

**AN EXPLORATION OF SYMPTOM BURDEN AMONG BREAST AND  
GYNAECOLOGICAL CANCER PATIENTS ACCESSING CARE AT UNIVERSITY OF  
ILORIN TEACHING HOSPITAL, ILORIN, KWARA STATE, NIGERIA.**

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## DECLARATION

I, ISIAKA-LAWAL SALAMAT AYODELE, hereby declare that the work on which this dissertation/thesis is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

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## ABBREVIATIONS

AIDS	= Acquired Immune Deficiency Syndrome
CT scan	= Computed Topographic Scan
ECOG	= Eastern Cooperative Oncology Group
ESAS	= Edmonton Symptom Assessment Scale
FAF	= Functional Assessment Flowchart
FIGO	= International Federation of Gynaecology and Obstetrics
HIV	= Human Immunodeficiency Virus
IQR	= Interquartile Range
KPS	= Karnofsky Performance Scale
MDASI	= MD Anderson Symptom Inventory
MSAS	= Memorial Symptom Assessment Scale
MSAS-GDI	= Memorial Symptom Assessment Scale- Global Distress Index
MSAS-PHYS	= Memorial Symptom Assessment Scale- Physical subscale
MSAS-PSYCH	= Memorial Symptom Assessment Scale – Psychological subscale
MSAS-SF	= Memorial Symptom Assessment Scale – Short Form
PMI	= Pain Management Index
SD	= Standard Deviation
SPSS	= Statistical Products and Services Solution
TMSAS	= Total Memorial Symptom Assessment Scale
TNM	= Tumour Node Metastasis
UTH	= University of Ilorin Teaching Hospital
WHO	= World Health Organization

## ABSTRACT

**Background:** Breast and gynaecological cancers are the leading causes of cancer morbidity and mortality among women in developing countries. Advanced stage diseases with limited availability for treatment imply significant symptom burden; the relief of which poses a challenge for the health care providers.

**Aim:** This study was conducted to measure symptom burden and relief among breast and gynaecological cancer patients accessing care in a tertiary health institution in Nigeria.

**Objectives :** 1) To determine the prevalence of symptoms among breast cancer and gynaecological cancer patients accessing care in UITH, Ilorin; 2) To determine the most distressing symptoms experienced by breast and gynaecological cancer patients accessing care in UITH, Ilorin and 3) To assess symptom relief in the two studied groups.

**Methods:** Both inpatients and outpatients with breast and gynaecologic cancers accessing care during the study period were recruited. All patients completed an interviewer administered MSAS-SF which assesses a 7-day prevalence and distress/frequency of 32 physical/psychological symptoms. Symptom relief was assessed 7 days later. Demographics, cancer stages, treatments received and palliative care referrals were obtained from the case notes. Karnofsky Performance Status Scale was used to assess functional status.

**Results:** Fifty breast and 49 gynaecological cancer patients were studied. Eighty percent of breast cancer and 91.9% of gynaecological cancer patients had advanced cancer. The overall mean number of symptoms was  $5.8 \pm 4.5$  for breast cancer while gynaecological cancers had  $8.1 \pm 4.6$ . The top 5 symptoms in breast cancer patients were pain (62%), worrying (44%), feeling sad (42%), weight loss (40%) and difficulty sleeping (38%). Gynaecological cancers had weight loss (67.3%), pain (65.3%), worrying (53.1%), feeling sad (51.0%) and lack of energy (46.9%) as the top 5. The most distressing symptoms were cancer-site specific such as fungating breast masses in breast cancer patients and vaginal bleeding/discharges in gynaecological cancer patients. Both groups similarly had pain and “don’t look like myself” as most distressing too. Symptoms reliefs were poor and comparable between the two groups and palliative care referrals were also generally low but worse among breast cancer patients. Gynaecological cancer patients had higher Global Distress Index (GDI= 0.88 Vs 0.48), were more physically distressed (MSAS-PHYS=



0.67 Vs 0.40) and had a poorer KPS ( $77 \pm 17.41$  Vs  $85 \pm 16.91$ ) compared to breast cancer patients.

Conclusions: This study shows higher symptom burden in gynaecological cancer patients, a comparably poor symptom relief in both groups and poorer palliative care referrals among breast cancer than the gynaecologic cancer patients. Gynaecological cancer patients had higher symptom prevalence and higher symptom distress scores and lower performance status compared to the breast cancer patients.

## Chapter 1

### INTRODUCTION

The majority of patients with breast and gynaecologic cancers in developing countries present with advanced disease (1)(2). The required specialists and facilities to manage these patients are either non-existent or not affordable if present, in countries such as Nigeria (3)(4). This implies that a large number of our patients will require palliative rather than curative treatments on first presentation. While it is important to improve prevention, early detection and treatment of cancer to be able to achieve a cure, it is also vital to provide palliative care to those who cannot be cured (5). The focus of palliative care research and development has mainly been on the prevalence and relief of pain. Cancer patients are known to have numerous other problems apart from pain (6). The generalist clinics and wards that characterize many hospitals in Africa are unlikely to meet the needs of cancer patients. Cancer patients here are seen alongside other patients with benign conditions and as such, the special attention and sensitivity that is required for their care may not be available. Even though it may not be feasible to change this arrangement now or in the near future, insights into the symptom experiences of women living with cancer will help to guide and improve services.

Clinical palliative care is essentially symptom oriented and symptom focused in its drive to improve the quality of life of patients facing life threatening conditions (7). Palliative care is relatively new in Nigeria and there is a need for clinicians to be familiar with the symptom pattern of cancer patients that are commonly encountered in this environment. Even though a palliative care team exists in the University of Ilorin Teaching Hospital, this team only sees patients that are referred to them and referral is at the discretion of the managing physician. Many patients with palliative care needs if not recognized by the attending physician and referred appropriately, will not be seen by the palliative care team. This study explores the symptom burden in women with breast and gynaecological cancers anticipating that the findings will better inform the managing doctors, the palliative care team and the hospital management on the needs and problems of these patients. This will serve as a guide for planning quality care that would help improve the quality of life of these patients.

## SYMPTOM AS AN OUTCOME MEASURE

The word 'symptom' is derived from the Greek word-symptoma- and it is translated as 'anything that has befallen one' (8). The dictionary defines symptom as "the subjective evidence of disease or physical disturbance observed by a patient" (9). The subjective nature of symptoms makes it an individualized entity even though the presence of a disease or its management or some other physical disturbances is central to its occurrence (10).

The presence of symptoms is a major reason for health care utilization by a large number of patients (11). Symptom management has gained much importance now than before because patients and other stakeholders are now more inclined to treatments or interventions that address symptoms (12). Symptoms have become equally important endpoints or outcome measure to consider when choosing between treatment options for cancer to the extent that it is now at par with other important outcome measures such as survival time, tumour size or time to recurrence which before now, were previously the only important outcome measures that are usually considered in patients undergoing cancer treatments (10).

Symptom burden portrays the cumulative effects of symptoms with their impact as it is observed or perceived by patients (12). A more comprehensive definition of symptom burden put forward by Gapstur (13) is "the subjective, quantifiable prevalence, frequency and severity of symptoms that place a physical burden on patients and may produce negative physical, psychological and emotional responses". The expression 'symptom burden' is said to be invented by physicians who also view and approach symptom burden differently (14). It is sometimes used synonymously with symptom distress (15). Symptom burden report is dependent on the perspective of whom it is viewed. Many have assessed symptom burden from patients' perspectives while others have done so from the health care providers' views or from the family carers' perspectives. Technically, symptom burden has been assessed through different modalities. Some have assessed it by simply noting the number of symptoms experienced by the patients (16) while others have assessed it by determining severity of the symptoms, allotting scores to the severity ratings and then adding up such scores to arrive at symptom burden assessment (17,18). Some others have incorporated functional interference in their assessment of symptom burden (10).

The importance of symptoms and the burden they constitute is continually been investigated by several authorities. Refinement in its definitions, the scope of its effects on patients and their families as well as the health care providers and the need to continually improve on its evaluation and subsequent symptom management will continue to be an open area of research.

## SYMPTOM BURDEN IN CANCER PATIENTS

Symptom burden in cancer patients is significant and symptoms are commonly present whether the cancer is amenable to curative treatment or the management focus will be palliative (19). While curative treatment is the focus of treatment in many illnesses, palliative care continues to be the main treatment modality in many chronic conditions including cancer (7). This is particularly so in developing countries where majority of cancer patients present at advanced stage of their disease (7). Cancer patients in developing countries are in a very precarious situation because they have a complex disease that often require multidisciplinary approach, requiring expertise that are often lacking in resource poor countries (3). Many cancer patients also usually traverse curative phase, palliative phase and subsequently, the end-of-life phase in the course of their illness. The transition through the phases may sometimes be dramatic and often unpredictable (20). Each of these phases of care is loaded with symptoms which often constitute significant burden to the patients with significant impact on patient well-being and quality of life. However, symptoms are often not explored and may often times go unnoticed by the health care providers (21). The magnitude of this symptom burden may be worse in developing countries where cancer treatment is most often suboptimal compared to developed countries (3). This unequal access to care is worse among the females in the developing countries compared to their counterparts in developed countries (22).

Breast and cervical cancers together are the major cancer resulting in death in women in the developing countries (23), both constituting a third and a quarter of all new cancer cases and cancer deaths respectively in women (24). In advanced stages, both of these cancers are characterized by symptoms whose profiles are poorly documented in Nigeria. This study has highlighted the symptom profiles of women with breast and gynaecological cancers and comparisons were made between the groups with respect to symptom experiences. The study was carried out in a tertiary health care centre which is a prototype of a typical highest level of

care such women can access in Nigeria. The symptom experiences were documented using a validated symptom assessment tool.

## GLOBAL CANCER BURDEN

The burden of cancer is commonly expressed as incidence, prevalence and mortality rates (25). The morbidity that accompanies cancer is usually not reflected in these statistics (26). However, more complex measures such as ‘‘disability-adjusted life years lost’’ and ‘‘persons-years of life lost’’ are the other estimates that attempt to describe the reduced quality of life and burden of disease experienced by the individual between diagnosis and death and also the impact of the disease on the society (25,27).

The World Health Organization (WHO) estimates in 2002 reported that 10.9 million new cases of cancer occurred worldwide while 24.6 million people were living with cancer and 6.7 million people died of cancer (28). It was projected then that the number of new cancer cases would increase from 10.9 million in 2002 to 16 million in 2020, with the number of deaths also increasing from 6.7 million in 2002 to 10.3 million in 2020 (28). Recent global cancer report is in line with these projections. In the year 2012, 14.1 million new cases of cancer and 8.2 million cancer deaths were recorded (24). The growing cancer incidence and deaths are occurring majorly in less developed countries as was predicted. There has been a generally rising trends in the number of cancer cases occurring in the developing countries (28). In 1970, only 15% of new cases of cancer were from the developing countries and this rose to 56% by 2008 (29). Recent global cancer estimates reported that 57% of new cases are from less developed countries and also, 65% of all cancer deaths were also from the less developed countries (24). The implications of all these are that more patients with cancers are to be expected to confront the health care services in the developing countries, further overstressing the limited resources.

## CANCER IN DEVELOPING COUNTRIES

Evidence of increasing proportion of cancers to occur in the developing countries abound (23,24,30,31). The reasons for these increases include aging population due to improved standard of living and increase in the adoption of cancer-associated lifestyles such as cigarette smoking and consumption of westernized diets (28,30). Improvement in the control of communicable diseases has also contributed to the apparent increase in cancer incidence (32). The truth

however is that most of developing countries are still battling with the double burden of disease - both communicable diseases like malaria and tuberculosis and the growing incidence of non-communicable diseases like cardiovascular diseases and cancer (33,34).

Sub-Saharan Africa is not prepared to face this growing disease burden (3). Comprehensive cancer care is still very difficult to be provided in many African countries because of poor health care systems that lack both the basic infrastructural facilities and the human resources (3,35,36). Health care policies are also not stable due to repeated disruption and fragmentations which sometimes result from political instability and conflicts (3,35). Even when higher numbers of cancer cases were reported for the developed countries, mortality rates for cancer were still disproportionately higher in the developing countries than the developed ones (23,28). Now that more cancer cases are to be expected from the developing countries, the resulting mortalities from cancers are likely to approach alarming proportions.

Cancer survival rates are also much lower in the developing countries compared to the developed countries (37). For example, the 5-year survival rate for breast cancer in some African countries is less than 50% while it is more than 75% in developed countries (23,37). The reasons for the lower survival are multiple. Lack of appropriate treatment due to lack of expertise and/or equipment, poverty and lack of appropriate cancer drugs are very common in the developing countries (28,36). Another important contributor to poor cancer survival in resource poor countries is the limited funding allotted to these areas (35,37,38). The shift in cancer burden to less developed countries has resulted in 80% of disability-adjusted life years been lost to cancer in these areas, yet only 5% of the world's resources to treat cancer are available here (35,37). These issues illustrate the task ahead for the developing countries if cancer survival is to be improved.

## CANCER SYMPTOM BURDEN IN DEVELOPING COUNTRIES

Cancer patients are known to experience significant symptom burden resulting from the disease, its management, and other non cancer morbidities or a combination of all these (39). Treatment related symptoms usually occur while on treatment but it may sometimes persist even after treatment had been discontinued or the cancer itself had been cured (12)(40). These varying

sources of symptoms require regular assessment and re-evaluation as well as comprehensive discussion about the symptoms with the patients (41). Continuing advances in treatment options for many cancers and discoveries of newer therapies all imply increases in cancer survivorship or disease free intervals, which may in turn signify the development of more treatment related symptoms (41). Many cancer patients in resource poor countries usually do not have access to either the conventional cancer treatments or the new emerging ones (42). The consequent of this is that the natural progression of the disease with its attendant symptom burden takes its natural toll on many of the patients. All the factors such as poverty, illiteracy and poor access to health care services that contribute to late presentation and eventual poor outcomes of the disease are particularly worse in women residing in resource poor countries (42-44). These women are culturally, educationally and socially disadvantaged compared to their female counterparts in the developed countries (22).

Breast and cervical cancers are the two most common female cancers in the developing countries (23,24). Breast cancer together with all the gynaecological cancers accounted for about 1.6 million out of the total of 3.8 million new cases of cancer in women in the year 2012 (24), constituting slightly over 40% of cancer cases that occurred in women. Over a quarter (28.3%) of all deaths from cancer in women were also attributable to breast and gynaecological cancers (24). Breast, uterine corpus and ovarian cancers were among the top ten new cancer cases in 2012 in both developed and the developing countries, with uterine cervix cancer been additional in the developing countries top ten cancer cases (24). The predicted increases in cancer incidence and deaths for the developing countries are becoming evident in the recent cancer statistic reports.

The rising trends in cancer cases in the developing countries are likely to soon overstretch the already meager health care systems which neither has the personnel nor facilities to handle them (45). Cancer screening services such as that of cervical cancer screening is an effective preventive measure that has helped in the drastic reduction of cervical cancer mortality in the developed countries (46). Such cancer screening services have been very difficult to establish in many developing countries like Nigeria because of the resources required for such services (46). But even if this and other preventive measures are established now, it is still unlikely that significant effects can be produced with respect to reduction in the number of cancer cases to be

expected for the next 10 years (28). Also, some cancers by virtue of their nature and location, coupled with some inherent patient factors, are not amenable to all preventive measures and continue to present in advanced stages for which cure is not possible and the patient will have to be palliated with symptomatic treatments only. With the present state of health care systems in many developing countries, symptom control by way of palliative care may be the only treatment available for many cancer patients in a long time to come.

## CANCER TREATMENT IN DEVELOPING COUNTRIES

In order to achieve a good treatment outcome in cancer care, a multitude of skilled specialists is required to make prompt and correct diagnosis which is followed by appropriate treatments including but not limited to surgery, radiotherapy, chemotherapy and supportive care (38). These are scarce commodities in the many developing countries. In Cameroun, there were only 2 oncologists to the 18.8 million populations as at 2010 (3). Similarly in Malawi, there was no trained oncologist in the whole country as at 2010 (47). According to WHO, Africa has less than 5% of the world's specialized health care workforce to tackle cancer (3,35). The necessary equipment to diagnose cancer such as CT scan, mammography and colonoscopy are also very limited (47). Radiotherapy capacity in Sub-Saharan Africa is grossly inadequate and unevenly distributed (48,49). Sixty percent of all the radiotherapy machines in Africa are found in Egypt and South Africa (48). Twenty-eight out of the 54 African countries lack radiotherapy facilities (49). In Nigeria as at 2008, there were 5 radiotherapy machines said to be available in the country (2). Considering the over 150 million population then, this is insufficient to serve the country. The recommended 0.4 radiotherapy machine per million of population is not likely to be met by many African countries (50). This gross shortage of radiotherapy facility is reflected in the long waiting list at the few radiotherapy centers available in Nigeria (2,48,49). The further implication of this for majority of the patients is the continuing disease progression resulting in worsening symptoms and symptom burden.

Cancer treatment and prevention have not been given as much attention as it should have because it is misconstrued to be a disease of the affluent while communicable diseases had more



attention in the developing countries (51). International finances to resource poor countries have been directed mostly on HIV/AIDS, malaria and tuberculosis (52) even though reports have shown that cancer kills more people than all these diseases combined (28). Evidence of relegation of cancer to the background is further reflected in the just concluded Millennium Development Goals where cancer care/control was not a prominent feature (53). The present Sustainable Development Goals may end up in similar fate for cancer care if no proactive steps are taken because all the competing diseases are still very much present. Lack of priority given to cancer care and control is contributory to poorly informed patients who present with advanced diseases.

Many cancer patients present very late in Africa. The knowledge about cancer is generally poor among the populace in the developing countries (54) and this implies poor preventive behaviors too (54). Limited resources contribute to poor availability of infrastructures, manpower, consumables, follow-ups and surveillance necessary for running many cancer screening programs (46). The few available services have been slow or fail to expand in many African countries (55). In Nigeria, cancer screening services are still poorly developed and the available services are underutilized (56-59). The lack of functional screening services contributes to advanced stages of disease that many patients present with. In a Nigerian study (43) on breast cancer patients, 75% of the patients presented with stage 3 or higher while in a similar study in Cameroun (44), 100% of the patients presented with similarly advanced stage of the disease. Both studies revealed that about half of the patients waited for more than six months with their illness before presenting to the hospital.

Several reasons are purported for the late presentation in these countries. These include belief in sorcery and witchcraft as the cause of the illness, poverty that make health care unaffordable, lack of early recognition and referral by the initial doctors and stigmatization sometimes associated with the disease (43). Seeking alternative treatments before resorting to orthodox medicine also contribute to delay in presentation with consequent advanced stage of the disease. The poor health care systems in many developing countries also contribute to the advancement of disease and eventual poor outcomes (4)(60). Early presenting cancers can still end up with poor prognosis because of poor accessibility or unavailability of health care services when needed. All these factors result in a vicious cycle of disease progression with consequent

increased cost of treatment which further impoverish the patients, increasing toxicity from treatment, greater disease and symptom burden, resulting in poorer treatment outcomes, shorter disease free intervals, lower survival rate and overall worsening of patients' quality of life (38).

## BREAST CANCER OVERVIEW

Breast cancer is the most common cancer in women worldwide, accounting for 25% of all cancers in women and 15% of cancer deaths (24). In Nigeria, breast cancer is also the commonest cancer in women (61), having overtaken cervical cancer (43,62). Despite higher incidences of breast cancer in the developed world, mortality is much lower than that in the developing countries, including Nigeria (62,63). Late presentation is a major problem in many breast cancer patients in developing countries and this has repeatedly featured in studies emanating from this part of the world (1,43,62,64). These studies have also shown that breast cancer in Black Africans tends to occur in premenopausal women compared to post-menopausal women in Caucasians. Also, the breast cancer in Africans is said to be more aggressive in behavior and are usually hormone receptor negative compared to the breast cancer types found in the Caucasians (64,65). Treatment for breast cancer, as with any other cancers in developing countries is suboptimal because of limited capacity for cancer care and poor awareness among the populace (4,45). A study (66) on the acceptance and adherence to treatments among breast cancer patients in Nigeria revealed that over a third of the patients declined any form of treatment and there was poor adherence to treatments with those on chemotherapy. These factors together with poor health care systems in developing countries imply significant residual disease with considerable symptom burden in these women.

Studies on symptom burden in breast cancer patients in this environment are very scarce. There are many studies (67-71) on the symptom burden in breast cancer patients in the developed countries but they are mainly on post treatment patients or those on treatments. Many patients in the developing countries are not on treatment because of illiteracy and poverty or unavailability of facilities and some others are sub optimally treated (4,47,66,72). The symptom profiles in the developed countries are likely to differ from those of the developing countries based on this difference alone.

Studies of breast cancer in Nigeria have been mainly retrospective. Many of the studies have looked at epidemiology of breast cancer with focus on prevention and possibly early detection to improve cure. Young age, premenopausal/peri-menopausal states of many women, relationship of the disease to parity, pregnancy and lactation and late presentations have been severally reported in many studies from Nigeria (1,64). Studies also abound on the histologic types of breast cancer in Nigeria with reports of the aggressive form being prevalent (64,65,73). Others have studied treatment challenges such as non-acceptance or non-adherence to treatment (66). Studies on the symptom profiles that characterize these women are poorly researched into. A few studies have mentioned the breast masses with fungating ulceration (74) and others have mention sites of metastasis and ensuing complications, but the symptom burden that accompany these pathologic states are rarely emphasized (1).

## GYNAECOLOGICAL CANCER OVERVIEW

Gynaecological cancers encompass a diverse group of tumours with different epidemiological features, clinical presentation and treatment strategies (27). Cancer of the cervix, body of the uterus, vagina, fallopian tubes, vulva and gestational trophoblastic tumours are all types of gynaecological malignancies (75). Cervical, uterine corpus and ovarian cancers are the most common gynaecological cancers worldwide (24). According to the 2012 global cancer estimates, there were 735,200 new cases of gynaecological cancers (cervical, uterine corpus and ovary) in the developing countries, constituting 19.2% of all cancers in women (24). This is double the incidence of cases in developed countries where only 9.5% of all cancers in women were of gynaecological origin (24).

Cervical cancer is the most common gynaecological cancer in the developing countries unlike developed countries where cancer of the uterine corpus is the commonest (24). It is the third leading cause of cancer deaths in women following breast and respiratory tract cancers (24). Uterine corpus cancer is next to cervical cancer in incidence in the developing countries and is closely followed by ovarian cancer (24). However, with regards to mortality, ovarian cancer is next to cervical cancer as leading cause of gynaecological cancer deaths worldwide as well as in

the developing countries (24). The other gynaecological cancers are relatively uncommon and do not feature in the leading causes of cancer incidences or cancer mortalities.

Studies on gynaecological cancers in Nigeria have been more of epidemiologic with reports mainly on the cancer types and presentations with respect to age, parity, advanced stages of diseases and treatment challenges (2,76-82). Cervical cancer has been reported to be the commonest gynaecological cancer in almost all studies in Nigeria. Some other studies have reported on the histologic types of the cancers (80). Like breast cancer, majority of gynaecological cancer patients in the developing countries report for diagnostic and treatment services at advanced stage of their disease. Most studies have reported on poor treatment outcomes as well as challenges with treatment in view of the very scarce radiotherapy facilities and prohibitive cost of effective chemotherapy (50). Surgical interventions are also of poor outcomes because of advanced stages of diseases and lack of expertise (83). A few studies (77) have reported on the clinical presentations of the gynaecological cancer patients. Ijaiya et al in their review reported on the symptoms documented in the patients' case notes (73). These include irregular vaginal bleeding, foul smelling vaginal discharge, weight loss, abdominal pain, urinary frequency, backache and hematochezia. Umezulike (84) also reported on similar symptoms in their study. No prospective study examining symptom burden in gynaecological cancer in Nigeria is available.

#### PALLIATIVE CARE AND CANCER CARE

Palliative care has been defined by WHO as an approach that improves the life of patients and their families, facing problems associated with life-threatening illnesses, through the prevention and relieve of suffering, the early identification and impeccable assessment and treatment of pain and other problems, physical, psychological, social and spiritual (85). Palliative care aims to reduce and possibly avoid the distress associated with terminal illnesses and helps to improve the quality of life of patients and their families (86). In many instances, cancer is a chronic illness which an afflicted person has to live with for sometime before death (86). The symptom burden during this period is usually enormous and most often challenging (86).

Cancer patients in resource poor countries often present in advanced stages of their disease for which palliative care is the care plan right from presentation (7,47). Even though cure is the

appropriate aim of medicine, Callahan et al has rightly acknowledged that other goals of medicine are equally important such as promoting health, preventing illnesses and injury and relieving suffering and caring for those who cannot be cured (5). Cancer and its incurability in some cases is a long known fact, yet palliative medicine which is most suited provision for it only developed a few years ago (87). Medical training of health care professionals is almost exclusively curative and at best preventive in focus and orientation (88). This cure-oriented model of training has produced physicians that lack palliative care and end-of-life care skills (89), yet significant numbers of cancer patients in resource poor countries require and can only get this type of care.

Palliative cancer care originated from developed countries and its effectiveness has been severally documented from those countries (89,90). Palliative care has attained much advanced stages of development in developed countries where integration into the health systems is common as well as recognition of palliative medicine as a specialty or subspecialty in medicine (89,90). These advances in palliative care in the developed countries are continuing despite the fact that cancer incidences are on the decrease, survival are better and treatment advances in cancer care is ever advancing in these countries. Developing countries on the other hand with the increasing cancer incidence, unavailability of cancer treatments and poor outcomes for cancer patients is yet to have palliative care readily available (90). This unavailability of palliative care is in spite of the relatively low cost and low technology required in the provision of palliative care (91). A few countries in Africa have actually made significant progress in palliative care development and integration into existing health care systems, but a larger majority of the African countries including Nigeria have not done so (92).

## Chapter 2

### LITERATURE REVIEW

This literature review was compiled by searching databases through Ebsco, Pubmed and Google Scholar platforms from University of Cape Town' health sciences library website. Chapters in books were also manually searched and Google Scholar searches. The words that were used for the searches include: cancer statistics, breast cancers, gynaecological cancers, cancer treatments, developing countries, Africa, symptom burden, symptom assessment, palliative care, and symptom assessment tools/instruments, developing countries, Nigeria, Africa and Sub-Saharan Africa. These words and phrases were variously combined in the search strategy.

### SYMPTOM PREVALENCE IN CANCER PATIENTS

Symptom prevalence studies have been conducted in various patient populations with cancer diagnosis. Yamagishi et al (93) studied symptom prevalence among cancer patients undergoing active anticancer therapy. The study consisted of patients with diverse cancer diagnosis but all commencing chemotherapy newly. Some other studies have been done on homogenous cancer populations, for example, Tasmuth et al (69) examined a cohort of early breast cancer patients that were exposed to surgical intervention. Barbare et al (18) on the other hand examined an extremely diverse patient population, consisting of patients with different cancer diagnoses, varied stages of disease, different treatment plans including curative, palliative as well as unclassified. Their large sample of over 45,000 patients also included patients with other non cancer morbidities as well as patients in different locations of treatments such as home care or hospital outpatients. Barbare et al's study is a population-based study that can only be conducted in countries with accurate medical recording systems including cancer registry. While such elaborate study may be difficult to replicate in developing countries where medical records including cancer registry are poorly kept, the large number of participants in this study makes it a valid study to refer to. These studies have all shown the ubiquitous dimensions of cancer patient populations that have been studied with the implication of extremely divergent outcomes that would be inherent to each and every study, given the varied patient populations, and varied stages of the diseases and treatments as well as different settings of studies. However, despite

these various cancer populations studied, comparative studies on symptom prevalence between different cancer types are not commonly available.

The symptoms reported in various symptom prevalence studies in cancer patients are quite different as would be expected from the cancer types apart from other differences like treatments or stages of the disease. A systematic review of the symptom prevalence and impact of multiple symptoms in cancer patients was carried out by Kim et al (94). The review reported on 18 studies involving a range of 26-527 patients. Fatigue, worrying, feeling nervous, dry mouth, insomnia, feeling sad/moody, feeling irritable, pain, drowsiness and distress in decreasing frequency were the 10 most prevalent symptoms reported. Fatigue was the most prevalent, occurring in 62% of the patients. An earlier but larger study by Saskia (95) on a similar group of patients reported 5 symptoms- fatigue, pain, weakness, lack of energy and lack of appetite as the most prevalent. Here again, fatigue was the most prevalent but together with pain were the only symptoms that were similar to both studies, showing differing symptoms reported. Kim et al examined only those studies that made use of 3 specific validated instruments while, the study by Sakia incorporated studies that extracted symptoms from questionnaires developed by the researchers and studies that used medical record documentations in addition to numerous other studies that used validated instruments . This probably resulted in the varying numbers of symptoms and the types of symptoms reported. In contrast to these two studies, Barbera et al (18) in their large statewide study in Ontario Canada, examined symptom prevalence in cancer patients using a single instrument to assess symptoms in over 45,000 patients. Report from this study was based on a 9-item symptom assessment instrument. Fatigue was still the most prevalent followed by poor well-being, poor appetite and being anxious. Again, fatigue is noted to be a common factor, but the other symptoms are different from those of the earlier studies.

It has been well acknowledged that cancer symptoms may result from the disease itself, the treatments side effects or complications from the treatments as well as from other possibly co-existing medical conditions (39). Symptom prevalence in cancer patients are likely to be influenced by these entities. Tasmuth et al (69) studied pain and other symptoms in 93 patients that had radical or conservative surgery for non-metastatic breast cancer. Even though some patients underwent other forms of treatment apart from the surgery, the main symptoms studied were exclusively in relation to the surgical intervention. The authors examine specifically

symptoms such as pain, oedema, numbness, weakness of arm phantom sensations in the removed breast and ipsilateral arm. This study overlooked other symptoms that may have arisen from chemotherapy, radiotherapy or a combination of these that some of the participants actually had. A similar study on patients receiving chemotherapy only, irrespective of initial cancer therapy was also conducted by Yamagishi et al (93). A total of 462 patients commencing chemotherapy newly were examined with questions that were relatively but not exclusively specific to chemotherapy-induced symptoms. The authors came up with 4 symptom clusters with the most frequently mentioned symptoms being oral problems, insomnia, psychological distress, severe fatigue, and severe appetite loss. The identified symptoms were more commonly associated with chemotherapy. These studies show that symptom prevalence study reporting on post treatment symptom experiences may vary greatly, depending on the treatments received by the study participants and the focus of the researcher.

#### SYMPTOM PREVALENCE STUDIES IN BREAST CANCER

Symptom prevalence studies in breast cancer patients like for any other cancers are also similarly done on patients that are either on anti-cancer treatment or in the post treatment period. Breast cancer treatments are basically surgery, chemotherapy, radiotherapy or hormonal therapy. Some patients undergo all these treatment modalities while some others have a selected combination of these. The majority of studies on symptom prevalence in breast cancer patients are from the developed countries where treatments are promptly administered unlike the developing countries where treatments are not readily available. While it cannot be assumed that treatment related symptoms in these studies are all attributable to the treatments received entirely, disease-related symptoms cannot always be discretely enucleated from patients' reports on symptoms in many of these studies.

A study on treatment-related symptoms in low-income women with breast cancer in California was conducted by Maly et al (70). All the women in the study were enrolled in a treatment program. They examined only 3 symptoms –depression, nausea and pain-in the study population of 921 women. These 3 symptoms were chosen because earlier studies in their environment had highlighted these to be the most prevalent symptoms in breast cancer patients undergoing



chemotherapy or radiotherapy. Depression was the most prevalent symptom but least recognized by the physicians, while pain and nausea were less common but better recognized by the treating physicians in that study. Even though low-income women in this study may be likened to women in the developing countries like Nigeria, only 3 symptoms examined in these women is too few to be compared in women from developing countries where disease burden of breast cancer is more. Sucala et al (96) investigating the role of multidimensional symptom and dysfunctional beliefs as predictors of quality of life in breast cancer patients on chemotherapy reported more elaborated symptom profiles. They reported on 145 breast cancer patients. An average of eleven symptoms was noted with a range of 0-26 symptoms. The most prevalent symptoms reported were dry mouth, lack of energy, numbness, difficulty sleeping, sweats, and body image issues, feeling sad and worrying. Gwede et al (97) conducted a similar study with respect to stage of disease and treatment status, and also using a similar assessment tool albeit slightly modified to that of Sucala et al. They explored symptom experiences in homogenous breast cancer patients and came up with 2 different patient subgroups- the low-symptom burden group and the high-symptom burden group. They reported on chills, emotional upset, change in taste, pain, muscle weakness, change in appetite, diarrhea, nausea, problem with urination and dizziness as the most prevalent symptoms in the high-symptom burden subgroup of patients identified in that study. These last two studies have examined patients with early stage breast cancer populations. Studies on a mixture of early and late breast cancer patients as well as on mixture of patients on treatment and those not on treatments that characterize many hospitals in developing countries are not commonly available. Knowledge of the symptom prevalence in these various mix of cancer patients is equally important especially for the generalist physicians who are the bulk of doctors that attend cancer patients in developing countries like Nigeria.

Tasmuth et al (69) studied 93 breast cancer women who had radical or conservative surgery for breast cancer. The authors examined symptoms one day prior to surgery and then at 3 other times postoperatively. While the symptoms assessed prior to surgery could have been very informative as far as pre-treatment symptom status was concerned, the authors seemed to have examined symptoms that were almost specifically associated with the surgical intervention that was planned. The study revealed more physical symptoms post operatively than pre-operatively. The symptoms reported on were restricted to pain, disturbed sleep, numbness, arm oedema, phantom sensation and muscle weakness which were all noted to be increased post operatively than pre-

operative. Anxiety and depression were however reported to be decreased post operatively than the prevalence noted before surgery. Chen et al (71) also looking at pre-surgical symptom profiles in early breast cancer patients as a predictor of quality of life 2 years later examined somewhat different but just 5 symptoms in a group of 198 Taiwanese women. The 5 symptoms which were extensively assessed using a structured questionnaire for each symptom were attentional fatigue, physical fatigue, sleep disturbance, depression and anxiety. These two studies examining similar patients with respect to stage of disease as well as surgical intervention have examined and produced divergence symptom profiles. Tasmuth et al(69) have examined symptoms from the view of effects expected from surgery while Chen et al have done so from the perspective of effects on quality of life. The possible symptoms that can be examined even in homogenous cancer patients are quite numerous. When other differences such as different disease stages or treatments given are considered, the list of symptoms would be even more incomprehensible for routine clinical use.

In an attempt to provide a collection of symptoms that would cut across breast cancer patients in different phases of the disease, Bender et al (98) did a composite study on breast cancer patients across the 3 phases of disease. The first phase consisted of patients who just had surgery for early stage breast cancer and had not commenced chemotherapy, the second phase study consisted of patients that have had both surgery and chemotherapy and some were on hormonal therapy while the third phase patients had metastatic disease. Symptom profiles for each of these phases were highlighted and symptom clusters for each phase were identified. A-thirteen item symptoms list used for the study was extracted from four different tools but some of the symptoms selected were still similar in meaning or closely related. For example, fatigue, feeling of lack of energy and decreased physical strength/weakness were listed as separate entities. The symptoms that cut across all the 3 phases in the study were fatigue, feeling depressed, feeling anxious, feeling of lack of energy, loss of concentration and weakness. Symptom prevalence in metastatic breast cancer was reviewed by Irvin et al (99) in an overview of symptom management in patients with metastatic breast cancer. Fatigue, depression, insomnia and pain were most prevalent symptoms in addition to metastasis site specific symptoms. The patient population in the third phase of Bender et al study (98) was those with metastatic breast cancer. The symptoms that were reported in this group of patients were feeling lack of energy, fatigue, feeling anxious, feeling depressed, difficulty sleeping and loss of concentration. Comparing the

symptoms in these two similar cancer groups, only fatigue, depression and insomnia were similarly reported by both authors.

Depression is a very common symptom among breast cancer patients in the literature. Maass et al (100) did a systematic review on the prevalence of depression and anxiety among breast cancer patients who were at least one year post diagnosis. They reviewed 17 studies and reported depression prevalence of 9.4 to 66.1%. They concluded that depression was commoner in breast cancer patients compared to the general population and that it persisted though of decreasing intensity over 5 years after diagnosis. This study however examined only those studies that recruited breast cancer patients treated with curative intents. They excluded those with advanced disease whose prevalence and trend of depression and anxiety may be different. Stafford et al (101) in Australia examined women with breast and gynaecologic cancer for depression at diagnosis and then followed them up for a year. Patients with anxiety, depression or both were more prevalent at diagnosis and the rate significantly reduced at 8 weeks and 24 weeks post diagnosis. The two patient groups were found to be significantly different with respect to marital status, location of residence and treatments received for their cancer. The stages of cancer which has important influence on symptoms were however not mentioned in that study and it would therefore be difficult to compare their findings with that of Tasmuth and Maas. The study however agreed with others that depression and anxiety improved over time in the study populations.

Each of these studies had reported on the different symptoms that were commonly observed in the different patient populations studied. Divergent as the symptom reports have been, they have helped to shed more light on the symptom profile possibilities that would guide in planning appropriate care and support to the diverse problems identified in patients studied.

## **SYMPTOM PREVALENCE IN GYNAECOLOGIC CANCERS**

Symptom prevalence studies in gynaecological cancers have been commonly done in the different individual cancers that are of gynaecologic origin. Many of the studies have been on

the most common cancers such as ovarian, cervical and uterine cancers. Patients on active treatment either primarily (102) or in clinical trial settings (103) were more commonly studied. Others were patients in the post treatment period or cancer survivors (100). Patients referred for palliative care interventions are another commonly observed group of patients for which symptom prevalence studies have been carried out.

Generally however, gynaecological cancers have some symptoms that may be common to them, while some other symptoms are peculiar with the specific cancer type. In a review of gynaecological cancers by Mishra (75), vaginal bleeding was reported to be the most common presenting symptom in cervical, endometrial and vaginal cancers, but less common with ovarian cancers. Other symptoms common to gynaecological cancers are vaginal discharge, constipation, diarrhea, nausea, vomiting and pain (75). Some pathologic states arising from genital cancers include symptomatic anaemia, obstructive uropathy, deep vein thrombosis, lymphedema, bowel obstruction, rectovaginal and vesicovaginal fistulae and a host of psychological issues (75)(84). All of these pathological states present with their unique symptoms.

Klee et al (104) in a study on cervical cancer patients' perspectives on physical symptoms after radiotherapy followed 118 patients for up to two years. There was a significant drop out of patients over time in that study but symptoms that were noted in the first 3 months after radiotherapy were diarrhea, nausea, and lack of appetite, frequency of micturition, dysuria, vaginal discharge, tiredness and weakness. The baseline symptoms prior to the commencement of therapy that would have made pre- and post-treatment symptoms better compared were not documented. Instead, a control group was used for comparison. All the symptoms listed were noted to be higher in the patients than the control group in the study. A baseline symptom profile could have provided symptom that could be attributable to the disease before onset of radiotherapy. Karin Ahlberg et al (102) in Sweden in a similar study but on patients treated with radiotherapy for uterine cancer, examined fatigue and a limited number of other symptoms. Their study aimed to explore the experience and relationship of fatigue and these other symptoms and also in relation to global quality of life for 60 patients referred for curative radiotherapy after surgery for uterine cancer. The symptoms selected were based on symptoms identified from other studies as being commonly associated with radiotherapy. Risk of

overlooking certain symptoms is present in this study especially if an assessment tool had not been used in identifying the key symptoms. The study examined fatigue, pain, diarrhea, loss of appetite, nausea/vomiting and insomnia at baseline and then at 3 weeks after commencement of radiotherapy and at the end of the treatment. They reported increase in all the symptom severity from baseline compared to subsequent measurements even though not all symptom differences reached statistical significance. Both of these studies have examined different cancer types exposed to radiotherapy. Symptom profiles in patients requiring radiotherapy and not getting it or receiving other forms of treatments instead of radiotherapy is also important especially for clinicians that practice in resource limited countries.

Symptom prevalence studies in ovarian cancer patients are commonly found in patients with advanced disease some of which may be undergoing clinical trials with chemotherapy. Jensen et al (105) studied 51 patients with stage 3 or 4 ovarian cancer with a newly developed 18-item symptom assessment tool. They came up with a number of symptoms and concerns reported by the patients. Fatigue, difficulty sleeping, constipation, nausea and pain were the top symptoms noted. Other concerns mentioned by the study participants were inability to enjoy life, varied contentment with quality of life, inability live an independent life, feeling ill and worrying that condition will get worse. Friedlander et al (106) in a multicenter study involving 18 centers across Australia and Canada examined symptom burden and outcome of treatment in patients with platinum resistant/ recurrent ovarian cancer. Patients were given palliative chemotherapy planned for a certain number of cycles, but more than half of the participant did not complete the cycles for reasons such death and adverse effects. The baseline symptoms that were commonly nominated by the patients were pain, fatigue, abdominal bloating, nausea, vomiting, bowel dysfunction, anorexia, hot flushes, dyspnoea and urinary problems. Emotional distress and insomnia were also mentioned. Donovan et al (103) did a systematic review to determine the recommended patient-reported core set of symptoms and quality of life domains to be used to measure in ovarian cancer treatment trials. The reviewed studies were from United States, Canada, Europe and Hong Kong. They identified abdominal pain, bloating, cramping, fear of recurrence/disease progression, indigestion, sexual dysfunction, vomiting, weight gain and weight loss as the core symptoms specific to ovarian cancer. Symptoms in ovarian cancer patients in developed countries are likely to be similar to that of the developing countries because ovarian cancers generally present in advanced stages anywhere (27) (105). However,

differences may be discovered between developing and developed countries with respect to adequacy of debulking surgeries and newer chemotherapeutic agents that may not be available to patients in the developing countries. These are important differences that may impact on symptom burden and may need to be explored in order to plan appropriate palliative/supportive care for ovarian cancer patients in developing countries like Nigeria.

A number of studies have also been done in gynaecological cancer patients referred for palliative care interventions. Kim et al (107) in their review of symptoms among advanced cervical cancer patients referred for palliative intervention reported pain, constipation and emotional distress as the most prevalent symptoms while anorexia, poor well-being, fatigue and insomnia were clinically significant symptoms as well. Aecke et al (108) in their review of 225 breast and gynaecological cancer patients admitted to a Palliative care unit of a University hospital in Germany reported weakness/vertigo, pain, anorexia, nausea and vomiting as the most common symptoms. Although the study was not a comparative one, the most prevalent symptoms among cancer groups were highlighted. Breast and ovarian cancer patients were most bothered by weakness/vertigo while cervical cancer patients had pain as the most prevalent symptom. Elumelu et al in a similar retrospective study (109) in palliative care patients in Ibadan, Nigeria also reported on breast and cervical cancer patients enrolled in the outpatient Palliative care services of a tertiary health care centre. Also not a comparative study, pain, vomiting, nausea and weight losses were the most common symptoms in both groups of women. Other symptoms similarly found in both patient groups were fatigue and lymphoedema. Chest symptoms (cough and dyspnoea) were exclusively found in breast cancer patients while gynaecological cancer patients exclusively had anorexia. Elumelu et al in the Ibadan study compared cervical cancer only with breast cancer patients. Even though cervical cancer is the commonest gynaecologic cancer in Nigeria as in other developing countries, uterine and ovarian cancers are also fairly common and ovarian cancer is particularly known for significant morbidity and mortality among the gynaecological cancers (27).

## SYMPTOM ASSESSMENT

Symptom assessment is a continuous process that is imperative right from the diagnosis of a disease condition and continues during monitoring of therapeutic interventions or disease

progression (110). The assessment of symptoms is a prerequisite for adequate and appropriate planning of quality care; yet comprehensive symptom assessment is not commonly performed in everyday clinical practice (17). Symptom assessment is important in cancer care because cancer patients frequently suffer from severe and multiple symptoms for which they seek symptom control with or without interventions for the underlying cancer. Symptom assessment like any other patients' needs assessment involves information gathering with the aim of identifying clinical needs that can be met (111). This information seeking requires a trusting relationship between the health care provider and the patient in order to be able to have an open and honest communication (120). Sophie et al(113) in a focused group discussion among health care professionals involved in cancer care at a University hospital in Sweden reported that striking up a relationship between the patient and the doctor is an important factor that influence symptom management. This relationship they further emphasized would only be created when doctors/nurses are readily available to attend to patients unhurriedly, individualize patients' care, instill confidence in patients as to the care to expect and encourage patients' participation in the care plan.

Clinical assessment of symptoms is confronted by a lot of challenges which constitutes barriers to good symptom control (114,115). Pain is the most studied symptom in clinical practice as well as in research settings. Problems and barriers to pain assessment and management have been severally studied and some successes have been reported (116). Even though pain management is not yet optimal (116), many lessons learnt from pain management so far can be extrapolated to other non-pain symptoms in cancer care.

## PAIN AS A PROTOTYPE UNDERTREATED SYMPTOM IN CANCER PATIENTS

Pain is one of the most feared and most burdensome symptoms in cancer patients (117). Pain is also one of the most prevalent symptoms in cancer populations. The prevalence of pain in cancer patients range from 30-60% in early stages of cancer and may rise to over 60% in patients with advanced cancer (118). Van den Beuken et al (117)in a systematic review on the prevalence of cancer pain in a varied cancer population reported a pooled prevalence of >50%, with the highest prevalence noted in head and neck cancer patients. Annelio Vamio (119) in a similar study on

symptom prevalence in patients with advanced cancer also reported prevalence of moderate to severe pain as 51%, ranging from 43% in stomach cancer to 80% in gynaecological cancers. Others have similarly reported pain as the most prevalent symptom (6) (120) or among the top five most prevalent (18) (95)(121) symptoms in their studies. It has been proposed that control of cancer pain should be feasible in up to 90% of cases (21) but this has not been the case. Despite research and guidelines on pain management, pain remains undertreated in both developed and developing countries (122,123). Pain in cancer is not physiologically different from those arising from other conditions, but the psychosocial and existential dimension to cancer pain makes it unique (112). Pain is also very important in that the presence of pain frequently influences the occurrence of some otherwise stand-alone symptoms such as sleeping disorders and depression (124).

In examining pain under treatment in Italy, Zenz (123) conducted a 3-year survey of the prescription pattern among German physicians. The study accessed 330 practices across Germany through computerized medical records of their prescriptions. The study revealed that only 1.9% of cancer patients were prescribed strong opioids and many of the prescriptions authorized inadequate dosing intervals. The study concluded that majority of cancer patients in Germany were not treated for pain at all and that those treated are grossly under treated. Andrea (21) in a systematic review of under treatment of pain examined 26 studies involving cancer patients. Pain Management Index (PMI) was used in assessing pain under treatment in this study. PMI relates the severity of pain report by patient to the level of analgesia prescribed by the physician. The authors acknowledged that PMI is a rough guide since other factors such as pathologic cause of pain, use of adjuvant or non-pharmacologic pain therapies or patients' compliant with treatment also influence adequacy of pain control. The study however concluded that nearly one of two patients (43%) with pain was undertreated. Apolone (125) in a multicentre study on the quality of cancer pain management in Italy reported lower overall prevalence of pain under treatment of 25% even though some of the centers had up to 55% prevalence. There seem to be a decreasing trend in the reported prevalence of cancer pain under treatment. A follow up study on that of Andrea was carried out by Greco et al (116). They systematically reviewed studies from 1994 to 2013, including that of Andrea; and further specifically reported on the prevalence of under treatment from 2007 to 2013. Twenty studies were reviewed from 2007 to 2013 and the mean prevalence of under treated cancer pain was 31.5% compared to



41.5% for the year 2001-2008. They reported a decrease in the prevalence of cancer pain under treatment to the tune of 25% at an approximately 1% decrease per year. Factors that were found to be predictive of pain under treatment were having a good performance status, early disease, minority groups or less educated individuals and when there is discrepancies between the patients' and the physicians' rating of severity of pain (21). Greco (116) also reported being managed in nonspecific settings as predictors of pain under treatment and this was similar to Apolone's(125) finding that patients in the palliative /hospice centers had better pain treatment than those in an oncology setting. It was unanimously agreed by many authors that under treatment of pain reported in many of the studies were attributed to inadequate pain assessment. These inadequacies were attributed to barriers that have been variously classified.

The barriers to symptom assessment have been classified as physician-based, patient-based and health care system-based (114,126). Malathi et al in their study to identify barriers to symptom management in a sample of 768 cancer patients in India classified these barriers as communication, personal, professional, financial and misconception barriers (127). Health-care providers contribute to inadequate symptom assessment in a number of ways. These include their training, their knowledge and their attitude (128). The cure-oriented background of physicians' training portrays diseases as having clear-cut pathophysiology with straight forward treatments (88). Symptoms whose pathophysiologies are uncertain constitute an uncomfortable zone for many physicians (88). The implication of this training is that unclear symptoms are not assessed and even when noticed, are not treated or are undertreated (21).

Poor knowledge is also a common reason for not assessing and treating pain among health care professionals. Devi et al (128) examined the barriers to cancer pain management among 253 doctors working in government hospitals in Sarawak, Malaysia. The study revealed that half of the doctors would not prescribe morphine for fear of respiratory depression, while over a third of them because of fear of addiction. The study concluded that knowledge about pain management was poor among the respondents and restriction on morphine was high. Liao et al in a similar study in China (129) examined assessment of cancer pain management among new fellows. Many of the fellows were of different disciplines like medicine, surgery, anaesthesia, ENT and paediatrics. The fellows reported that their training in cancer pain management was poor and this they linked majorly to poor pain assessment skills. Result from the survey revealed that barely

half (49%) of the physicians correctly responded to clinical scenarios on management of cancer pain.

Attitude and behavior of health workers are also recognized barriers to symptom assessment. The assumptions that patients would volunteer symptoms without being asked leave many symptoms unaddressed (126). Bias of treating similar cases differently can be attributable to individual doctor's attitude (130) and this can significantly impact on patients' symptom management.

Patient-based barriers to pain assessment are also enormous. The assumption by the patient that the doctor should know that symptoms are present in them is quite common (126). Others include fear of addiction to opioids, worrying about side effects of drugs, financial constraints to buy prescribed drugs and misconception about drugs for pain (126,127). Fear of disapproval by doctor or family carer and not to be seen as ungrateful also constitutes a common barrier to symptom reporting (126). Studies have also reported that patients may not report symptoms for fear of being disqualified from clinical trials (131).

Institutional barriers to pain management were elaborated by Kwon et al in their review (115). Inadequate availability of medications especially opioids and poor interventional pain services due to lack of expertise and equipment was highlighted in the review. Lack of support services from specialists in pain and palliative care and psychosocial supports services were also identified as important barriers to pain management. Anorlu (2) in her review of cervical cancer in sub-Saharan Africa noted that poor co-ordination across multiple care providers is also a commonly reported challenge in cancer care because many of specialists needed in cancer care in Africa for instance, work in isolation. In many health institutions, poor staffing with high patient load per doctor or nurse, lack of privacy due to overcrowded wards and clinics gives little time for adequate patient evaluation for symptom assessment (126).

#### **SYMPTOM ASSESSMENT BY PATIENT, CARER OR HEALTH CARE PROVIDER**

Symptom assessment is central to symptom management in cancer care (132). The subjective nature of symptom means there are multiple ways of assessment as well as method of checking symptom reports with more objective means (133). However, patients' self-report of their symptom experiences are still considered the most appropriate means of assessing symptoms and are superior to proxy assessments (110). Nekolaichul et al (132) in a prospective study of 49

patients with advanced cancer compared symptom assessment by a proxy such as a doctor or nurse and that of the patients themselves. The study reported that both doctors and nurses more often underrated patients' symptoms but the underrating was worse by doctors than the nurses. Oechsle et al (134) in a similar study incorporated family member in the comparison. Their own study reported that physicians underrated symptoms while family members on the other hand overrated the patients' symptom severity. Nekolaichuk and Silveira et al (132,135) studied these proxy assessments over time in order to discover a trend but noted no improvements. Oechsle et al (134) further examined dimensions of frequency, intensity and distress to each symptom as a pointer to treatment indication. They discovered that treatment indication was based on symptom intensity and not frequency. Inaccurate symptom assessment by proxy therefore could have significant implications leading to overtreatment or inadequate treatment of symptoms.

Many symptom assessment tools are designed for patients to respond (135) while some others are constructed for the carer to respond (136). Proxy symptom assessments are sometimes necessary because cancer patients, especially in the advanced stages may be too ill to engage in conversations or may be cognitively impaired by their disease to engage in any meaningful communication (132).

Symptoms harvested from symptom assessment are dependent on several factors. These factors include patients' factors, disease factors, the informant's factor as well as the method or tool that is used to obtain such information. Un-captured symptoms will continue to infringe on the patients' comfort and reduce quality of life. While little can be done to patients' and disease factors, a lot could be done to improve the methods of collection of this vital information in order to improve on care and support to be provided.

## SYMPTOM ASSESSMENT TOOLS

A symptom diary which captures the daily fluctuations of symptoms and has potential to reduce recall bias is said to be the gold standard for symptom record but, this method of symptom assessment is not acceptable for many patients because of the burden it imposes on them and the high rate of non compliance by the patients (110). Symptom assessment tools in the form of questionnaires are better alternatives to diary recordings (110). The tools are structured

documents containing the list of symptoms to be assessed and how they should be assessed. Availability of these tools should help to improve symptom assessment and subsequent management but this is yet to be generally acceptable to all health care providers.

The use of symptom assessment tools in eliciting symptoms in patients is evidenced based but unlike other evidence based clinical practices, it is yet to be widely accepted by health care providers (137). Many healthcare professionals have not adopted the use of symptom assessment instruments despite the evidences from research that have shown that structured interviews are more accurate in eliciting symptoms(138) and lead to better symptom control as well as better improvement in the quality of life of patients(139). Reasons that have been reported for poor compliance with the use of these tools by the health care providers include concern over the clinical practicability, burden of such measurements especially in busy clinics and uncertainties/unacceptability of its usefulness or importance (137). Others have reported poor clarity on its use and the processes involved; some see it as an abnormal way of eliciting symptoms from patients while difficulty in the interpretation of the scoring systems/scales was also seen as an issue by others (140).

Bainbridge et al (141) surveyed the perception of 128 health care professionals on the use of a symptom assessment tool (ESAS) in a regional cancer centre in Ontario, Canada. The survey revealed that nearly half of the physicians do not agree that ESAS would enhance patients' care and a noticeable number expressed that the tool was of no benefit to them in usage. Pereira et al (142) in a larger but similar study on same issue surveyed 960 health care providers in 14 regional cancer centers also in Ontario. Their report was that of significant discrepancy between the health care workers' attitudes to the use of symptom assessment tool and the reported actual use of the tool (ESAS). They also reported that about one third of the respondents do not refer to the tool while 44% believe in taking their own history from patients for assessing symptoms.

Until more efforts are directed at combating these concerns, the acceptance of the symptom assessment tools by the healthcare professionals may remain poor.

Symptom variability occurs in response to treatments or as disease progresses (143). These symptom changes may have implication for the tools to be used if comprehensive symptom assessment is to be achieved (143). While the use of one symptom assessment over time allows

trends in symptoms changes to be glaring, this may not be appropriate all the time (144). Lasheen et al (144) in a study on symptom variability in hospice patients reported apparently static symptom prevalence over 5 consecutive days. The median number of symptoms at admission and 5 days afterwards was 4, but the quality of the constituent symptoms differed. The number of participants in the study also decreased over the time of study with 125 enrolled and 30 completing the study in the 5 days. A similar study by Spichiger et al, examining symptom changes over a 10 day period in similarly hospitalized cancer patients reported an average of 13 symptoms at admission and 9.3 symptoms 10 days later (145). Also, number of participants decreased from 103 to 53. The patients in both studies were comparable but the number of symptoms reported differed greatly. The symptom assessment tool used in eliciting symptom prevalence is a key determining factor of the symptoms to be elicited. The earlier study by Lasheen et al assessed only 6 symptoms albeit through 2 different methods while the later used MSAS which consisted of 32 symptoms. Variability of symptoms could also be viewed from the perspective of the actual symptom changes apart from number. The development of new symptoms and disappearance of others as was demonstrated in both studies constitute symptom variability that may have implication for the symptom assessment method or tool to be used to capture these changes. The single assessment tool used throughout the course of symptom monitoring in both studies may also explain some drop out of patients who became too sick to continue with the study for which a different method or tool may have been more appropriate to use.

To further demonstrate the changes in symptom quantity and quality with the commencement of treatments and the effect of the assessing tool, Spichiger et al (146) studied symptom changes over 3 months in cancer patients commencing chemotherapy with the aid of MSAS. The study reported high symptom prevalence prior to treatment and further hike in the number of symptoms with commencement of treatments, but symptom scores for each individual symptom greatly varied both within and between individual patients over time. Yamagishi et al (93) in similar study looked at the dimension of symptom distress using Distress Thermometer and then symptom number, by using MDASI. They reported decrease in distress caused by the symptoms over time and increase in physical symptoms only in those with increased symptom distress. Both of these studies have shown difficulty in comparing outcomes even in similar patient populations being assessed for similar parameter. This difference may probably be because of the

different assessment tools employed in the studies. The need to individualize symptom assessment with respect to patients' needs as they arise and the need to identify the appropriate tool to use to capture these changes as they arise is important in symptom prevalence studies. A symptom assessment tool that has an adequate amount of the symptoms that are commonly observed in cancer patients would be better at capturing symptom changes.

#### The Memorial Symptom Assessment Scale (MSAS)

The original MSAS consisting of 33 symptoms was developed by Portenoy et al and the reliability and validity of the tool was evaluated in cancer patients in 1994 (147). It is a symptom assessment tool with multidimensional measurement of each symptom. Further revision of the original tool resulted in the present 32 symptoms now present consisting of 28 physical symptoms and 4 psychological symptoms. The tool has an allowance of 2 optional symptoms to be added if present. Twenty-four symptoms are assessed by their frequencies, severities and the degree of distress they cause using 4 or 5 Likert scales. The remaining 8 symptoms for which frequency of occurrence seem inappropriate such as weight loss and hair loss were assessed with respect to severity and how much they caused distress. All symptoms were assessed based recall period of the preceding one week. The 28 physical symptoms are assessed for degree of distress or bother they constitute. The frequency of occurrence and the severity of the symptoms are omitted. The 4 psychological symptoms are assessed for the frequency of occurrence only. The shortened form ensures that patients' burden in completing the form is reduced and also the time to completion is shorter (148).

The MSAS-SF has been shown to be equally valid and like the revised MSAS, further subscales can be obtained from it (148). The Global Distress Index (MSAS-GDI) is a 10 item composite consisting of 4 psychological symptoms (feeling sad, feeling irritable, worrying and feeling nervous) and 6 physical symptoms (lack of energy, lack of appetite, pain, feeling drowsy, constipation and dry mouth) it measures the overall symptom distress. The MSAS-GDI has been found to be clinically relevant as it correlates predictably with quality of life and patients' clinical status (147). The physical symptom subscales (MSAS-PHYS) is obtained from the average score of 12 prevalent physical symptoms. These are lack of appetite, lack of energy, pain, feeling drowsy, constipation, dry mouth, nausea, vomiting, change in taste, weight loss, feeling bloated and dizziness. The scaling of the degree of distress for each symptom is in 0.8,

with 0 being no symptom, 0.8 for symptom present but causing no distress, up to maximum of 4 for symptom causing very much distress.

The psychological symptom subscale (MSAS-PSYCH) is obtained from the average scores of 6 prevalent psychological symptoms. These are worrying, feeling sad, feeling nervous, difficulty sleeping, feeling irritable and difficulty concentrating. The scoring for the psychological symptoms is in increments of 1, with 0 being no symptom at all and 4 for the symptom that is almost constantly present. The total MSAS score is the average score of all the 32 symptoms present in the MSAS-SF.

MSAS-SF was chosen for this study because of its broader number of symptoms, its ease of completion and the several subscales that can be derived from it. Although it has not been validated in African settings, it also being used in African studies (6) (149). It has been translated into several African languages in the studies that used it among cancer population (6).

#### Edmonton Symptom Assessment Scale (ESAS)

The original ESAS was constructed by Bruera et al in 1991(150). It was construed to be used frequently in palliative care setting and could be completed by the patient themselves or with the help of a nurse or relative (150). It consisted of 8 symptoms initially but it was later increased to 9 with further allowance of one additional optional symptom to be added if present (151). The original tool was a visual analogue scale of 10-100mm but further modification was done to create the 11-point numerical scale from 0-10 (152). Synonyms for some of the symptoms were also introduced, for example, tiredness/fatigue. This was done to increase its acceptability and usability by patients (153). The 9 symptoms contained in ESAS are pain, tired, nausea, depression, anxiety, drowsiness, appetite, well-being and shortness of breath (154).

Most of the studies that used ESAS in symptom assessment were done in Canada, United States of America and other similarly developed countries (152). None seem to have been done in African settings (155). The visual analogue format and the numerical rating scale style of this tool also makes it not appropriate for African setting where many patients are illiterates and may find it difficult to comprehend (41). A categorical grading of symptom will be more appropriate in this environment. The very few number of symptoms assessed also made it inappropriate for use here. These were the reasons why the tool was not selected for this study.

## MD Anderson Symptom Inventory (MDASI).

MDASI consists of 13 symptoms that are rated on an 11-point scale from 0-10, with 0 meaning “not present” and 10 indicating “as bad as you can imagine” (17). It also has 6 interference items to indicate how the presence of the symptoms interferes with other aspects of normal living (17). These interference items are also rated from 0-10, with 0 meaning “did not interfere” and 10 meaning “interfere completely” (156). The 13 core symptoms are: fatigue, disturbed sleep, distress, shortness of breath, drowsiness, dry mouth, sadness, difficulty remembering, numbness or tingling, lack of appetite, nausea and vomiting (156). The interference items are in relation to others, enjoyment of life, mood, walking, general activity and working (156). The combination of symptom severity and the interference are used to measure symptom burden.

The primary MDASI was designed for 24 hour recall of symptoms, but other time periods such as the previous one week is said to be available on request (156). The tool is very easy to use and can be completed in 2-5 minutes (126). There are also various means of administering MDASI. It is available in pencil and paper format, interactive voice response system, tablet PC and also web-based applications (156).

MDASI was not chosen for the study because it requires an undisclosed amount of money to be paid to the authors before it can be used (156). It also involves protocols and permission before it can be translated it can be translated to local languages (156). MDASI has also not been used in an African setting (157) unlike MSAS.

## Karnofsky Performance Scale (KPS)

Performance status is an estimate of a patient’s level of functioning with regards to carrying out daily activities and self-care (158) (159). It assesses the level of independence a patient possesses and determines how much activities such individual can perform by themselves (158).

Performance statuses have been shown to correlate with symptoms and certain symptoms are associated with poor performance status (160,161). The performance status is also useful in much clinical decision making including recruitment for clinical trials (162). It is an important



determinant of treatment commencement, continuation, interruption as well as termination and these in turn impact on survival and quality of life (162).

There are various instruments that are also available for measuring performance status, but the two commonly used are the Karnofsky Performance Scale (KPS) and the Eastern Cooperative Oncology Group (ECOG)(163). A new instrument called the Functionality Assessment Flowchart (FAF) has recently been developed also for assessing performance status in cancer patients (162). It is a modification of both KPS and ECOG and said to have higher inter-observer agreements than the previous two (162). KPS was chosen for this study however because of its long standing use in clinical practice. It is a clinician-rated performance scale and consists of 11-point rating scale from normal functioning scored as 100 through to 0 score for dead.

## RATIONALE FOR THE STUDY

Many cancer patients have to cope with this significant symptom burden. Pain and other symptoms experiences by cancer patients in Africa are poorly researched (164) and the unaddressed symptoms continue to contribute to poor patients' and their families' satisfaction with health care services. Data on symptom prevalence other than pain are scarce in many developing countries. Most of the available studies are on symptom prevalence in cancer patients from the developed countries and these cannot be assumed to be similar to ours because of differences demographics, culture and health care systems (6). Breast and gynaecological cancer are the major killers of women in Nigeria (165,166). Hospital based mortality records in Lagos, Nigeria reported breast cancer as the most common cause of death (165). A similar review on mortality from the gynaecological unit of a similar tertiary health care centre in Nigeria reported that 88% of deaths from the gynaecological unit were from cancer cases and the remaining 12% were from benign conditions (166). The prevalence and burden of symptoms in these major women killer diseases are insufficiently documented. In Nigeria, most of the studies in the women have been mainly retrospective with focus on clinical presentations (77,167), identification of risk factors (64), treatment outcomes (62,66) and challenges of management (66)(83) . No study has examined the symptom prevalence prospectively nor has any study been done on the groups of women using a validated symptom assessment tool. The aim of this study was to explore and compare the symptom experiences among breast and gynaecological cancer patients in a tertiary health care institution with the view to identify their symptom burden and make comparison that will inform future management decisions and lead to overall improvement in the care given to help improve on the quality of life of the patients.

## **AIMS AND OBJECTIVES**

### **AIM:**

To explore and compare the prevalence of the different symptoms among breast cancer and gynaecological cancer patients accessing care in University of Ilorin Teaching hospital (UITH).

### **OBJECTIVES:**

1. To determine the prevalence of symptoms among breast cancer and gynaecological cancer patients accessing care in UITH, Ilorin.
2. To determine the most distressing symptoms experienced by breast and gynaecological cancer patients accessing care in UITH, Ilorin.
3. To assess symptom relief in the two studied groups.

## **Chapter 3**

### **METHODOLOGY**

#### **STUDY DESIGN**

The study was a comparative descriptive cross-sectional hospital-based survey.

#### **STUDY SITE**

The study was conducted at the surgical outpatient and gynaecology outpatient clinics and the corresponding inpatient wards of the University of Ilorin Teaching Hospital, Ilorin, Kwara State of Nigeria.

#### **STUDY POPULATION**

The study population was all eligible breast cancer and gynaecology cancer patients admitted into the female surgical ward and gynaecology ward and also similar patients attending the respective outpatient clinics. The study was conducted from 20<sup>th</sup> October 2015 to 15<sup>th</sup> of April, 2016.

#### **SELECTION CRITERIA**

The following were the inclusion criteria for the selection of participants:

1. Confirmed breast cancer or gynaecology cancer
2. Patient over 18 years of age

The following were the exclusion criteria for the selection of participants:

1. Patients who were in extreme distress such that communication was not possible.
2. Patients who were unable to give consent, for example, an unconscious patient.

## **SAMPLE SIZE**

The sample size calculation was based on the equation developed by Robert Lehr (168) to estimate sample size for two study groups.

$$(n): n = (16SD^2)/D^2$$

Where n is the estimated sample size per group,

SD is the projected standard deviation of the mean (in this case 7 from previous study (6)),

and D is the desired, or clinically important, difference between the two groups (D=4).

Assumes that  $\alpha$  (or the P value) is 0.05, that  $\beta$  is 0.20 (power of 80%),

$$n = 16(7^2)/4^2$$

$$=49$$

Sample size of at least 49 was used per group.

## **STUDY SAMPLE**

There was no sampling done in the study but all eligible patients that were attending UITH for care as either outpatient or inpatients were enrolled. All eligible patients were enrolled as they presented to the hospital until the desired sample sizes were reached for both groups of patients.

## **STUDY PERIOD**

Recruitment of patients for the study begun on the 20<sup>th</sup> October 2015 and the last patient was recruited on the 15<sup>th</sup> April, 2016.

## **DATA COLLECTION**

### **Data Collection Tools**

The data collection tool consisted of three parts: 1) a participant data sheet; 2) the Memorial Symptom Assessment Scale Short Form (MSAS-SF); 3) the Karnofsky Performance Status. The

MSAS-SF was used during the initial interview with the patient and again at the second interview with the patient.

#### 1) The Participant data sheet

This was used to record the socio-demographic details of the participant. Information for this sheet was obtained mainly from the patient's case notes with occasional supplemental information from the patient. The socio-demographic details obtained included the age, religion, educational level, ethnicity, occupation and phone numbers. Other details obtained were the type of cancer, the duration of disease as recalled by the patient, the stage of the disease, and indication for present admission (for in-patients), both current and previous cancer specific and non cancer specific treatments received and involvement or non-involvement of hospital palliative care team in the management. The staging systems for breast and gynaecological cancer are different. The breast cancers were staged using the Tumour, Node and Metastasis (TNM) staging systems. The gynaecological cancers were staged by FIGO staging systems for the various gynaecological cancer types. Both the TNM and FIGO systems stage cancers from 0/1 to 4.

The participant data used for this study was a modification from a similar study in the literature (3).

#### 2) The Memorial Symptom Assessment Scale Short Form (MSAS-SF)

This is a validated tool for symptom assessment and it was used to document symptoms that the patient had experienced in the preceding seven days prior to the interview. The original MSAS tool was developed by Portenoy et al in 1994 (147) and has been validated in cancer patients. The MSAS-SF is a modification of the original tool and it has also been validated among cancer patients in New Jersey in the year 2000 (148). It has not been fully validated in Africa or Nigeria, but a pilot study of MSAS-SF was conducted in Uganda (169). MSAS-SF has also been used in several African studies (6) (169). The MSAS-SF is a 32-item validated assessment tool containing 28 physical symptoms and 4 psychological symptoms. It has space for additional symptoms that may be present but not included in the list. Participants are required to answer yes to symptoms that are present and then go further to state how much the symptom bother or distress them for physical symptoms; and for psychological symptoms, patient are to state how

often the symptoms occurred. The distress levels of the physical symptoms are recorded on a five point Likert scale of 0.8 to 4 at an incremental rate of 0.8 i.e individuals whose symptoms did not bother them at all, those with a little bit of bother, those somewhat bothered, those bothered quite a bit and those very much bothered are scored, 0.8, 1.6, 2.4, 3.2, and 4.0 respectively. The frequencies of the psychological symptoms are also recorded on a four point Likert scale of 1 to 4. Those whose symptoms rarely occur are scored 1, those with occasional symptoms are scored 2, those with frequently occurring symptoms are scored 3 and those with almost constantly present symptoms are score 4. The MSAS sub-scales which are the physical subscales (MSAS-PHYS), psychological subscales (MSAS-PYSCH), and the global distress Index (GDI) are obtained from selected symptoms from the MSAS. The detail of these symptoms and the scoring method is illustrated at the appendices.

The MSAS-SF was translated into Yoruba, Igbo and Hausa languages. The translation into Yoruba and Igbo languages was done by Dr Adeyemi and his colleagues of the department of Language of the University of Ilorin while the Hausa translation was done by Mr Jibril of department of Hausa at the Ahmadu Bello University, Zaria. The translation was done into these languages and back to English language to check the accuracy of the translation. These are the three main languages in Nigeria. The MSAS-SF and the participant's data sheet were pretested on 4 patients at the nearby general hospital in the state. Three breast cancer and one gynaecology cancer patients were used for the pretest. The pretest showed the need to include telephone number in the study proforma and it further confirmed that the whole interview process takes between 10-15 minutes. The MSAS-SF was interviewer administered in order to cater for some patients that may be illiterate and also to keep the information as uniform as possible.

- 3) The Karnofsky Performance Status was used to assess the functional status of the patients. It is an 11-point scale from 0% to 100% with 0% being dead and 100% being normal functional status. This assessment was done by observing the patient and also asking questions related to activities of daily living. This assessment was carried out by the researcher alongside the interviewing process.

## **Data collection process**

### Introduction to the study site

Having obtained ethical approval from the University of Cape Town, faculty of health Sciences, Human research Ethics Committee, the University of Ilorin teaching hospital ethical board and permission from the respective heads of departments, the researcher introduced the research to other key consultants and matrons in the clinics and wards. The clinics were such that 2 or 3 different clinics were run at the same time with the patients all sitting in same area. The Surgical Outpatient clinic for instance had orthopaedics, cardiothoracic, paediatric surgery and urology clinics all alternating sharing of clinics with the general surgery clinics. The general surgery clinics are the places to identify breast cancer patients and breast cancer patients are just a proportion of their overall patient load. Since there are no breast oncologists, all the general surgeons attend to all breast cancer patients on all their different clinic days. The gynaecology clinics were less cumbersome but since there were also no gynaecology oncologists, all gynaecological cancer patients were being attended to by the gynaecologists in their different clinic days. The general surgery clinics were run by mornings while gynaecology clinics run in the afternoons. The wards were much calmer and serene and the matrons in charge were more constant and easily approached. They were informed about the study and their cooperation was given.

### Recruitment of participants

Participants were recruited while they were waiting to be seen by their doctors at their respective clinics. In the clinics, the matrons in charge of the case notes were approached for case notes of general surgery patients or gynaecology patients respectively and assisted in identifying patients who met the selection criteria. Potential participants were approached individually and invited into a private room where they were informed about the study and invited to take part in the study. They were informed about the aims and conduct of the study and were told that their participation was voluntary and that if they choose not to take part in the study, they would not be penalized in any way. They were assured of confidentiality and were told that their participation would not interfere with their being attended to by their original doctors. They were informed that they would be interviewed now and then again in a week or two either by another



physical encounter or via telephone. Those who agreed to participate were then given patient information sheet to read and take away. The content of the information sheet was explained to those who could not read using the language of their choice which were English, Yoruba, or Hausa. Those who chose to participate were asked to sign or thumb prints a consent form.

#### Data Collection Method

The participant's data was first extracted from the case notes with occasional confirmation from the patients. A separate notebook was used to obtain the patients' name, hospital number and the assigned study number only. Thereafter, the MSAS-SF was administered by the researcher in the language of their choice and the participants' responses were documented. Each participant was asked for the presence or absence of the symptoms in the last one week and the degree to which they were bothered or distressed by each of the physical symptoms and the frequencies of the psychological symptoms.

After completing the MSAS-SF, the researcher then rated the patient's functional status by observation and also asking some activity related questions. The Karnofsky performance score was allotted as appropriate. The participant was thanked for taking part in the research and was reminded that she would be seen or spoken to again.

The fourth part of the assessment was the repeat of the MSAS-SF after an average of 7-12 days. This second contact with the patients was done by telephone contact because majority of the patients were seen at the outpatient clinics. Having noted the status on treatments, the second contact was to assess relief of symptoms or changes in the symptoms using the MSAS-SF as a check list with reference to the previously mentioned symptoms. A new MSAS-SF form was used for the second interview. New symptoms were noted and recorded as for first time while the previously noted symptoms were noted for degree of relief described as totally relieved, significantly relieved, slightly relieved, same or worse. No scoring was allotted to this grade of relief. Several calls were made before some could be spoken to again. This resulted in varied

interval of one week to 4 weeks between the first and second contacts. Some patients were lost to the study and not contactable even after several attempts at calling.

### **Data storage and confidentiality**

The notebook containing the participants' names and numbers and the consent forms were kept separately and away from participants' data sheets and the two MSAS-SFs. Completed data sheets were kept in a locker by the researcher in her personal library. Data were entered into the researcher's personal computer which is pass-warded. The note book containing the participants' names and hospital numbers with the allotted study numbers was also kept in the researcher's personal library and separate from the data sheets.

### **DATA ANALYSIS**

Data collected on a designed proforma was sorted and manually checked for data clarity and errors before entry by the researcher. Data were entered into SPSS version 20.0 (Statistical Products and services Solution formerly called statistical package for social services [IBM-SPSS inc Chigaco, II, USA version 20.0]). Data exploration was also done to ensure accuracy.

Tables and graph was used to report descriptive statistics. Categorical variables such as patients' demographic information, stage of disease and symptoms documented among the two groups of patients was presented as proportions and frequencies.

Categorical variables like patients' demographics, stage of disease and symptom burden was compared using Pearson's Chi-squared test or Fisher's Exact test to test for significant association between these variables. Fisher's exact test was used if the expected cell frequencies were below 5.

For continuous variables, means, median and standard deviations and interquartile ranges (IQR) were computed. The continuous variables were observed for normality with the aid of histograms

or boxplots. Student's t-test was used to test for significant association between the continuous variables with normal distribution while those with skewed distribution had the level of significant association tested for by the Mann-Whitney test. The following continuous variables: age, number of symptoms, duration of symptoms, MSAS-PHYS, MSAS-PSYCH, and TMSAS were compared between the groups. The level of significance was set at  $p \leq 0.05$ .

## **ETHICAL CONSIDERATIONS**

The study obtained permission from the Human Research Ethics Committee of the University of Cape Town and the ethical committee of University of Ilorin Teaching hospital, Ilorin, Nigeria.

The heads of departments of Surgery and Gynaecology were both approached after obtaining the ethical approvals. A letter of permission with the attached letter of approval from the ethical committee was submitted to each of the departments and their heads were also physically seen afterwards to further brief them on the study. They both passed the information to their other consultants in their various departments. The hospital palliative care team was also informed about the study and their support and co-operation sought.

The study involved no direct intervention to the participants and so there were no obvious risks to the patients. However, patients with cancer are considered vulnerable by virtue of the nature of their disease. This study population therefore required additional protection. This was ensured by affirming the ability of the patients to communicate for a period of 10-15 minutes from the ward nurses in the case of the inpatients and from the accompanying relatives for the outpatients. For patients that looked frail, the interview was maintained at a pace they could cope with. These patients may also be considered vulnerable because of the power imbalance in patient-doctor relationship which may put patients under pressure to accept to participate in research against their wish. This was eliminated from this study because the researcher introduced herself as a doctor who does not work in the hospital. The patients were also told that they were being seen by the permission of their primary physicians who is responsible for their care entirely.

The study was of some benefits to some of the patients. The study was an opportunity for some patients to know about palliative care. Occasional patients with palliative care needs when identified were discussed with the primary physicians. The physicians then refer the patients to the palliative care team.

## Chapter 4

### RESULTS

#### Sociodemographic information

The study was conducted among 99 cancer patients. Fifty (50.5%) of them were breast cancer patients while 49(49.5%) were gynaecology cancer patients (Table 1). All were accessing care at the University of Ilorin teaching hospital as either outpatients or inpatients. Of all the patients approached for the study, one patient refused and gave no reason for her refusal. Table 1 shows summary of the socio-demographic information of the study population. The overall mean age of the study population was 55.23+ 13.12; median age was 56 years and the age range was 25 to 85 years. About two-thirds (63%) were Muslims and the remaining were Christians. A little over a third (36.4%) of the patients had no formal education while about a quarter (26.3%) of them had tertiary level of education.

Table 1: Socio-demographic information of the study population

Factor	N (%)
Age	
Mean $\pm$ standard deviation	55.23 $\pm$ 13.12
Median	56.00
Range	25-85
Educational level	
None	36 (36.4)
Primary	20 (20.2)
Secondary	17 (17.2)
Tertiary	26 (26.3)

Religion	
Islam	63 (63.6)
Christianity	36 (36.4)
Diagnosis	
Breast cancer	50(50.5)
Gynaecologic cancer	49 (49.5)

### **Age Distribution by diagnosis**

Gynaecology cancer patients were older than the breast cancer patients with a peak age incidence of 60- 69 years while breast cancer patients had peak age incidence of 40-49 years, figure 1. The mean age for breast cancer patients was  $52.76 \pm 13.51$  while the mean age for gynaecology cancer patients was  $59.78 \pm 11.85$ . The difference in the mean ages between the two groups was statistically significant ( $p= 0.008$ ). However, there was no significant difference in the peak age group,  $p= 0.171$

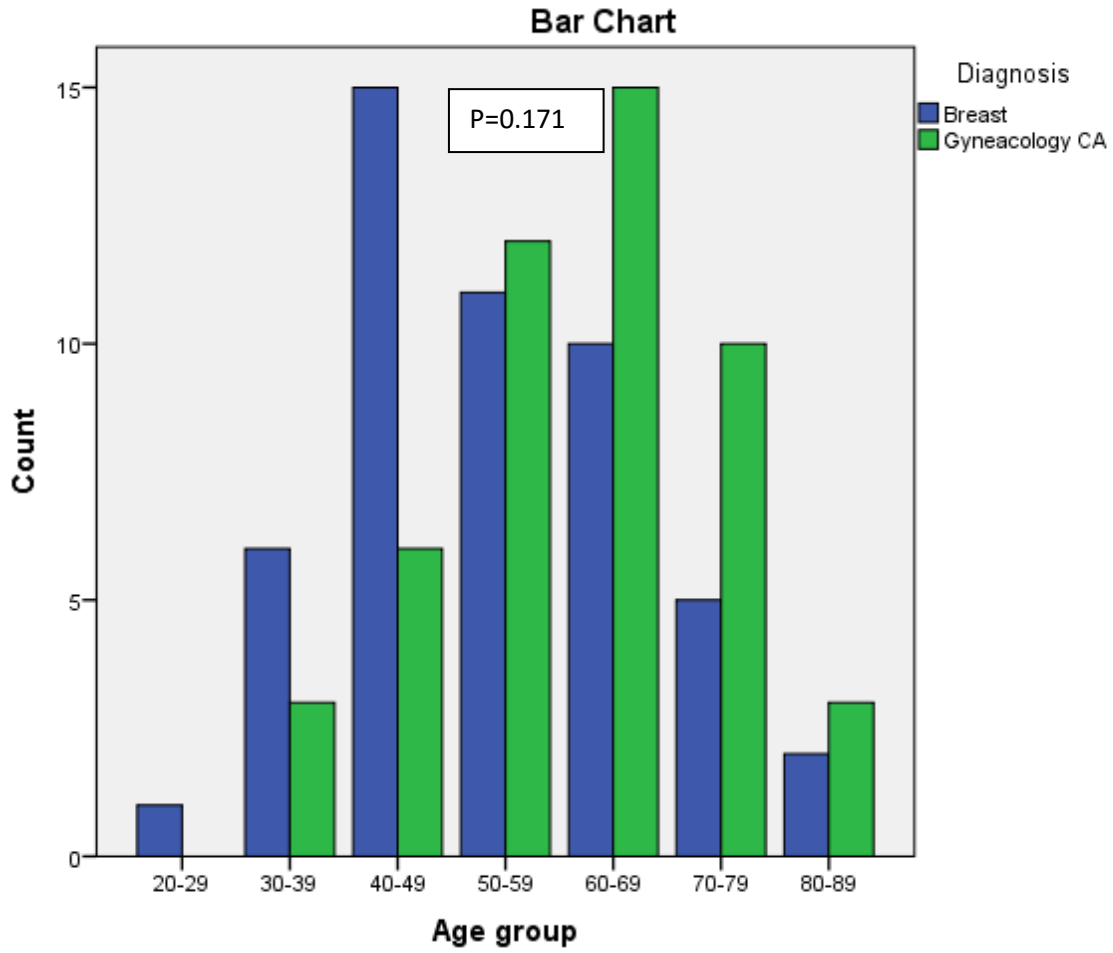


Figure 1: Age distribution and peak ages for breast and gynaecology cancer patients.

### **Educational Status by diagnosis**

Table 2 shows the educational status of the participants. Breast cancer patients were more educated than the gynaecological cancer patients with half (50.0%) of them having at least a secondary school level of education while only about one third (36.7%) of the gynaecologic cancer patients had at least, a secondary school level of education. The differences in the educational levels between the two groups were not significantly different ( $p=0.331$ ).

Table 2 : Educational status of participants in the two groups

Educational level	Breast cancer	Gynaecological cancer	P-value
None	17(34.0%)	19(38.8%)	0.331
Primary	8(16.0%)	12(24.5%)	
Secondary	8(16.0%)	9(18.4%)	
Tertiary	17(34.0%)	9(18.4%)	
Total	50	49	

### **Stage of disease by diagnosis**

Table 3 shows the stages of the diseases at the time of interview in the two groups. At least 80% of both groups of patients were seen with at least stage 3 diseases. The stages of the disease were not statistically different between the two groups ( $p=0.241$ )

Table 3: Distribution of stage of disease by diagnosis

Stage of disease	Breast cancer n (%) (TNM staging)	Gynaecologic cancer n (%) (FIGO staging)	P-value
Stage1	2(4.0)	0(0.0)	0.241
Stage 2	8(16.0)	4(8.2)	
Stage 3	29(58.0)	36(73.5)	
Stage 4	11(22.0)	9(18.4)	
Total	50	49	



Table 4 shows the educational status by stage of disease of the participants. More of the patients with no education (92%) and those with primary level (100%) presented at advanced stage of their disease (stages 3 and 4) than the more educated patients with secondary school (58.8%) and tertiary level (84.6%) and this was statistically significant ( $p= 0.02$ ). However, the highest proportion (30.8%) of tertiary education level patients had stage 4 disease compared to all the other lower levels.

Table 4: Educational level by stage of disease for all the participants

Educational level	Stage 1	Stage 2	Stage 3	Stage4	Total	p- value
None	0	3	27	6	36	0.02
Primary	0	0	17	3	20	
Secondary	1	6	7	3	17	
Tertiary	1	3	14	8	26	
Total	2	12	65	20	99	

### Location of patient

Table 5 shows the location of patient for the interview. Majority of the gynaecological patients were seen as inpatients while most of the breast cancer patients were seen at the outpatient clinics. The difference in the inpatient/outpatient status between the two groups was statistically significant with more gynaecological patient being inpatients ( $p=0.000$ ).

Table 5 Location of patient at the time of interview

Inpatient/outpatient	Breast cancer n (%)	Gynaecological cancer n (%)	P-value
Inpatient	5(10.0)	24(48.9)	0.000
Outpatient	45(90.0)	25(51.9)	
Total	50	49	

### **Involvement of palliative care team**

Table 6 shows involvement of palliative care team at the time of the interview. More gynaecological cancer patients were being seen by the palliative care team than the breast cancer patients, but the difference between the two groups was not statistically significant ( $p=0.121$ ).

Table 6: Involvement of palliative care team in patient management in the two groups

Involvement of Palliative team	Breast cancer n (%)	Gynaecological cancer n (%)	P-value
Yes	3(6.0)	8(16.3)	0.121
No	47(94.0)	41(83.7)	
Total	50	49	

### **Treatment Status**

Table 7 shows the status of treatment. Over 90% of gynaecological cancer patients were not on any treatment at the time of the interview while only one third of breast cancers were not on treatment. Of the 10 that had completed treatment among the breast cancer patients, 7 were still on hormonal treatment and follow up; two had completed hormonal therapy for 5 years and was just on follow up and 1 had exhausted all available cancer treatments options. Gynaecological cancer patients that had completed treatment also had exhausted all the available treatments options. Majority of breast cancer patients had ongoing cancer treatment which was mainly chemotherapy and/or hormonal therapy and a few were perioperative. Of the 15 breast cancer patients not on any anti-cancer treatment, 5 had financial constraints in procuring chemotherapeutic drugs, 6 were awaiting palliative surgery, 4 were admitted for correction of anaemia, and one was admitted due to respiratory distress. Of the 46 gynaecology cancer patients not on any anti-cancer treatment at the time of the interview, 9 were awaiting chemotherapy, 11 were awaiting surgery, 11 were already referred for radiotherapy but yet to go and 15 were still being evaluated. The difference in the treatment status between the two groups of patient was statistically significant ( $p=0.000$ ).

Table 7: Status of treatment at the time of interview in the two groups

Status of current treatment	Breast cancer n (%)	Gynaecologic cancer n (%)	P-value
Ongoing	22(44.0)	0(0.0)	0.000
Abandoned	1(2.0)	0(0.0)	
Completed	10(20.0)	3(6.1)	
Interrupted	2(4.0)	0(0)	
Not on treatment	15(30.0)	46(93.8)	
Total	50	49	

#### Duration of disease by diagnosis

Table 8 shows the duration of disease as at the time of interview. The median duration of disease for breast cancer patients was 12 months (6-25) while it was 7 (5-16.5) months for gynaecology patients. The median duration of disease was statistically different between the two study populations ( $P=0.022$ ). More gynaecology patients were within six months of their disease than breast cancer patients (48.9% versus 26%) but this difference was not statistically significant ( $p=0.071$ ).

Table 8: Duration of disease in the two groups of patients

Duration of disease	Breast cancer n (%)	Gynaecologic cancer n (%)	P-value
Less than 6 months	13(26.0)	24(48.9)	0.071
7-12 months	15(30.0)	13(26.5)	
13-24months	10(20.0)	7(14.3)	
25- 36 months	4(8.0)	0(0.0)	
More than 36 months	8(16.0)	5(10.2)	
Total	50	49	

Table 9 shows the duration of symptoms by the educational levels of the participants. The mean duration of symptoms among the participants were not significantly different between the different education levels ( $p=0.318$ ).

Table 9: Mean Duration of disease by the educational levels of the participants

Educational levels	Number	Mean	Standard deviation	95% confidence interval for mean		p-value
				Lower bound	Upper bound	
None	36	15.2	15.0	10.1	20.3	0.318
Primary	20	14.1	15.9	6.6	21.5	
Secondary	17	22.5	26.8	8.7	36.3	
Tertiary	26	22.7	25.3	12.5	32.9	
Total	99	18.2	20.6	14.1	22.3	

**Comparison of number of symptoms, MSAS subscale scores and KPS between the study groups.**

Table 11 shows the average number of symptoms, the MSAS subscale scores and the Karnofsky Performance Scores in the two groups. The number of symptoms on the MSAS-SF (which consisted of 32 symptoms) range from 0-17 for all patients and when additional symptoms (extra 1 - 3 symptoms) were considered, the number of symptoms ranged from 0-18.

The overall number of symptoms for breast cancer patients ranged from 0-18 while it ranged from 0-17 for gynaecologic cancer patients. The mean number of symptoms for breast cancer patients was less than that of gynaecologic patient ( $5.48 \pm 4.21$  versus  $7.12 \pm 4.64$ ,  $p=0.068$ ). This difference did not reach statistical significance. However, with additional symptoms (MSAS plus), the mean numbers of symptoms for Breast Cancer was significantly less than that of the symptoms for gynaecological cancer patients ( $5.82 \pm 4.50$  versus  $8.06 \pm 4.63$ ,  $p=0.016$ ).

Gynaecological cancer patients had higher scores for two of the MSAS subscales as shown in table 10. MSAS-PHYS (p=0.001) and GDI (p=0.040) subscales were significantly different between the two groups. The MSAS-PSYCH (p=0.216), TMSAS (p=0.054) and TMSAS with additional symptoms (p=0.234) were comparable between the two groups.

Table 10: Average number of symptoms, the MSAS subscales scores and the Karnofsky Performance Scores in the two groups of patients

Parameter (Mean±SD)	Breast cancer	Gynaecological cancer	P-value
Number of symptoms on MSAS-SF	5.48 ± 4.21	7.12 ± 4.64	0.068
Total number of symptoms with additional(MSAS-SF plus)	5.8 ± 4.5	8.1 ± 4.6	0.016
TMSAS (without additional symptoms)	0.41 ± 0.36	0.56 ± 0.41	0.054
#TMSAS (with additional symptoms)	0.88 ± 0.72	0.70 ± 0.39	0.234
Karnofsky Performance Status	85.80 ± 16.91	77.35 ± 17.41	0.016
Parameter (Median, IQR)			
GDI	0.48(0.06-0.98)	0.88 (0.28-1.27)	0.040
MSAS-PHYS	0.26(0.00-0.63)	0.53(0.24-1.27)	0.001
MSAS-PSYCH	0.40(0.00-1.06)	0.67(0.00-1.50)	0.211

SD=standard deviation; IQR=Interquartile range

# TMSAS = computed only for the 50 patients with additional symptoms

### Karnofsky Performance Status

The Karnofsky performance status (KPS) for this study population ranged from 40-100%. The mean KPS for breast cancer patients was significantly higher, 85.80 ± 16.91 compared to 77.35 ± 17.41 score for gynaecological cancer patients (p=0.016). More breast cancer patients, 20 (40.0%) had almost normal scores compared to gynaecologic cancer patients 6 (12.2%) (Table 11).

Table 11 Karnofsky Performance Statuses of patients in the two groups

Karnofsky Score (0-100)	Breast cancer n (%)	Gynaecologic cancer n (%)	p-value
Disabled (40)	2(4.0)	1(2.0)	0.007
Requires considerable assistance (50)	3(6.0)	7(14.3)	
Requires occasional assistance (60)	0(0.0)	6(12.2)	
Cares for self (70)	6(12.0)	5(10.2)	
Normal with effort (80)	7(14.0)	7(14.3)	
Normal activity, minor signs/symptoms (90)	12(24.0)	17(34.7)	
Almost normal (100)	20(40.0)	6(12.2)	
Total	50	49	

### Comparison of symptoms prevalence by diagnosis

The leading symptoms among the study groups were different and also, the differences in the prevalence of some symptoms were significant between the two groups (Table 12). In the breast cancer patients; pain (62.0%), worrying (44.0%), feeling sad (42.0%), weight loss (40.0%) and difficulty sleeping (38.0%) were the top 5 symptoms while in the gynaecologic patients, weight loss (67.3%), pain (65.3%), worrying (53.1%), feeling sad (51.0%) and lack of appetite (49.0%) were the top 5 . There were a number of additional symptoms which were not listed in the MSAS-SF but frequently described by the gynaecological cancer patients. These were mainly vaginal bleeding and discharge and they were actually the most frequent symptoms in the gynaecology patients (69.4%).

Symptoms with significant differences in prevalence between the two groups were: weight loss ( $p=0.006$ ), lack of appetite ( $p\leq 0.0001$ ), hair loss ( $p\leq 0.0001$ ), change in taste ( $p=0.012$ ), constipation ( $p\leq 0.000$ ), nausea ( $p=0.041$ ), problem with urination ( $p=0.001$ ), feeling bloated ( $p=0.031$ ), and the additional symptoms 1 and 2, not listed in the MSAS-SF ( $p=0.000$ ,  $p=0.031$ ).

Patients were asked whether they had additional symptoms and to mention these symptoms. The additional symptoms were different in the two study groups and they were frequently mentioned. In the breast cancer group, 16 patients mentioned additional symptoms 1: breast masses with or without ulcerations (7), breast discharges (1), chest discomfort (2), neck/axillary masses (2), and hoarseness of voice (1), muscle cramps (1), shivering (1) and amenorrhoea (1). Additional symptoms 2 were mentioned by 4 patients: abdominal discomfort (1), bed sores (1), breast wound (1) and immobility (1). Among the gynaecologic cancer group, 34 patients had one additional symptom: vaginal bleeding (18), vaginal discharge (7), abdominal swelling (3), gait problem (1), headache (1), vulva swelling (1) and continuous leakage of urine (1). Additional symptom 2 was mentioned by 12 patients: vaginal discharges (11) and discharging vulva sinuses (1).

Table 12 Comparison of symptoms prevalence in the two groups

Symptoms	Breast n/50	Gynaecology n/49	Total n/99	p-value
Pain	31(62.0%)	32(65.3%)	63(63.6%)	0.732
Weight loss	20(40.0%)	33(67.3%)	53(53.5%)	0.006*
Additional 1	16(32.0%)	34(69.4%)	50(50.5%)	0.000*
#Worrying	22(44.0%)	26(53.1%)	48(48.5%)	0.367
#Feeling sad	21(42.0%)	25(51.0%)	46(46.5%)	0.368
Lack of energy	17(34.0%)	23(46.9%)	40(40.4%)	0.190
Difficulty sleeping	19(38.0%)	21(42.9%)	40(40.4%)	0.622
Lack of appetite	8(16.0%)	25(51.0%)	33(33.3%)	0.000*
Numbness/tingling in hand and feet	13(26.0%)	16(32.7%)	29(29.3%)	0.467
Don't look like myself	11(22.0%)	14(28.6%)	25(25.3%)	0.452
Cough	12(24.0%)	11(22.4%)	23(23.2%)	0.855
#Feeling nervous	10(20.0%)	12(24.5%)	22(22.2%)	0.591
Dry mouth	8(16.0%)	11(22.4%)	19(19.2%)	0.415
Hair loss	18(36.0%)	0(0.0%)	18(18.2%)	0.000*
Additional 2	4(8.0%)	12(24.5%)	16(16.2%)	0.031*

Shortness of breath	10(20.0%)	6(12.2%)	16(16.2%)	0.295
Change in taste of food	3(6.0%)	12(24.5%)	15(15.2%)	0.012*
Constipation	1(2.0%)	14(28.6%)	15(15.2%)	0.000*
Dizziness	7(14.0%)	8(16.3%)	15(15.2%)	0.747
Swelling of arms/legs	8(16.0%)	6(12.2%)	14(14.1%)	0.592
Nausea	3(6.0%)	10(20.4%)	13(13.1%)	0.041*
Sweats	9(18.0%)	3(6.1%)	12(12.1%)	0.121
Problem with urination	0(0.0%)	10(20.4%)	10(10.1%)	0.001*
Feeling drowsy	6(12.0%)	3(6.1%)	9(9.1%)	0.487
Feeling bloated	1(2.0%)	7(14.3%)	8(8.1%)	0.031*
#Feeling irritable	4(8.0%)	4(8.2%)	8(8.1%)	1.000
Difficulty swallowing	3(6.0%)	4(8.2%)	7(7.1%)	0.715
Vomiting	1(2.0%)	6(12.2%)	7(7.1%)	0.059
Change in skin	4(8.0%)	1(2.0%)	5(5.1%)	0.176
Itching	3(6.0%)	2(4.1%)	5(5.1%)	1.000
Problem with sexual interest/activity	1(2.0%)	1(2.0%)	2(2.0%)	1.000
Difficulty concentrating	1(2.0%)	0(0.0%)	1(1.0%)	1.000
Diarrhea	0(0.0%)	1(2.0%)	1(1.0%)	0.310
Mouth sores	0(0.0%)	0(0.0%)	0(0.0%)	-

# refers to psychological symptoms \* refers to significantly different symptoms (P-value less than 0.05)

### **The topmost distressing symptoms in the two groups**

The highly distressing symptoms for the physical symptoms were those that were rated as “quite a bit” or “very much”, while psychological symptoms reported as “frequently occurring” or “almost constantly occurring” are considered highly distressing. The most distressing symptoms for this study are those for which at least, 50% of the patients rated them as “quite a bit/very much” and “frequently occurring/almost constantly occurring” for physical and psychological symptoms respectively. Symptoms that were experienced by only 1 person in either group were



excluded from this analysis. These were constipation, feeling bloated, vomiting, problem with sexual activity/interest, difficulty in concentration and diarrhea.

Table 13 shows the topmost 5 distressing physical symptoms for breast cancer patients. ‘‘Don’t look like myself’’ (72.7%) and pain (54.8%) were the highly distressing symptoms from the list of 28 physical symptoms listed in the MSAS-SF. The other symptoms rated as highly distressing were the additional symptoms (75.0%) not listed in the MSAS-SF and they include fungating breast masses or ulcerations, neck swelling and immobility. Swelling of arms/legs and some other additional symptoms were among the 5 leading most distressing symptoms but they occurred in less than 50% of those with the symptoms. All of the psychological symptoms were not considered highly distressing because all of them were rated as rarely or occasionally occurring.

Table 13 The top five most distressing symptoms among breast cancer patients

Symptom	Not at all/little bit (%)	Somewhat (%)	Quite a bit/Very Much (%)
Pain	9 (29.0)	5 (16.1)	17 (54.8)
*Additional 1	2 (12.5)	7 (43.8)	7 (43.8)
Don’t look like myself	1 (9.1)	2 (18.2)	8 (72.7)
Additional 2	1 (25.0)	0 (0.0)	3 (75.0)
*Swelling arms/legs	5 (62.5)	0 (0.0)	3 (37.5)

\*= among top five but not significantly distressing in up to 50%

Table 14 shows the topmost distressing symptoms among the gynaecological cancer patients. The most distressing symptoms among the gynaecologic cancer patients for which >50% of the patients rated as ‘‘quite a bit/very much were problem with urination (70.0%), don’t look like myself (64.3%), difficulty sleeping (57.1%), and pain (50.0%). The additional symptoms rated as

highly distressing (over 70.0%) included vaginal bleeding, vaginal discharge, abdominal swelling, vulva swelling, discharging sinuses and abnormal posturing. All the psychological symptoms were also not rated as highly distressing.

Table 14 the topmost distressing symptoms among the gynaecological cancer patients

Symptom	Not at all/little bit (%)	Somewhat (%)	Quite a bit/Very Much (%)
Pain	7(21.9)	9(28.1)	16(50.0)
Additional 1	2(5.9)	7(20.6)	25(73.5)
Difficulty sleeping	3(14.3)	6(28.6)	12(57.1)
Don't look like myself	2(14.3)	3(21.4)	9(64.3)
Additional 2	0(0.0)	1(8.3)	11(91.7)
Problem with urination	2(20.0)	1(10.0)	7(70.0)

### **Symptom relief among the study population**

Symptoms relief or improvement was assessed after at least 7 days from the first contact. The period ranged from 7 -33 days with a mean duration of  $8.86 \pm 3.5$  days. A total of 8 patients were not reachable for the second contact. One died (a gynaecological cancer patient) before the minimum of 7 days required for contact while the remaining 7 (4 breast cancer patients and 3 gynaecological cancer patients) were not reachable by phone or physical contact.

Symptom relief or improvement resulting from usual treatments provided by patients' usual attending physician was assessed. Some patients had been treated for symptoms such as pain with analgesics, all anemic patients had been transfused and some patients, especially the breast cancer patients had been commenced on chemotherapy before the time of second contact.

Some patients reported new symptoms not mentioned at the first contact. The new symptoms included 3 new cases of pain, 2 new cases of lack of energy, a patient reported difficulty sleeping

and 2 patients reported diarrhoea. Three other symptoms were not listed in the MSAS-SF (vaginal discomfort, vaginal bleeding and yellowness of the eyes).

Table 15 shows the comparison of relief or none relief of the symptoms assessed between the two groups of patients. Symptom relief was considered to be present when at least 50% of the patients with the symptom reported relief/improvement. There were poor symptom reliefs for the physical symptoms in most patients. Among breast cancer patients, 28 physical symptoms (excluding mouth sores and including the two individualized additional symptoms) were assessed for relief/improvement, only 4/28<sup>a</sup> symptoms: constipation, itching, problem with sexual interest and difficulty with concentration were reported as relieved by at least 50% of those affected. Gynaecological cancer patients on the other hand had 27 symptoms assessed (excluding difficulty in concentration and hair loss but including the individualized additional symptoms). Only 2/27<sup>b</sup> symptoms (dizziness and itching) were relieved in at least 50% of those with the complaint.

The only 2 (feeling irritable and feeling nervous) out of the 4 psychological symptoms were relieved/ improved in at least 50% of those affected among breast cancer patients while less than a third(18-26%) of those with psychological symptoms were relieved/improved of their symptoms among the gynaecological cancer patients. The differences in relieve of all the symptoms between the two groups of patients was not statistically significant ( $p \geq 0.05$ ).

Table 15 Physical and psychological symptoms relief among the study populations.

Symptoms	Breast Cancer n (%)		Gynaecological cancer n (%)		P-value
	Relieved	Unrelieved	Relieved	Unrelieved	
Pain	10(33.3)	20(66.7)	8(27.6)	21(72.4)	0.632
Additional 1	3(17.6)	14(82.4)	6(18.8)	26(81.3)	1.000
Weight loss	0(0.0)	17(100.0)	1(3.3)	29(96.7)	1.000
*Feeling sad	8(40.0)	12(60.0)	6(26.1)	17(73.9)	0.515
*Worrying	8(40.0)	12(60.0)	6(26.1)	17(73.9)	0.515
Lack of energy	3(16.7)	15(83.3)	5(23.8)	16(76.2)	0.702
Difficulty sleeping	5(27.8)	13(72.2)	4(21.1)	15(78.9)	0.714
Numbness/tingling in hand and feet	5(45.5)	6(54.6)	4(26.7)	11(73.3)	0.419
Lack of appetite	1(16.7)	4(83.3)	6(28.6)	15(71.4)	1.000
Cough	3(25.0)	9(75.0)	0(0.0)	9(100.0)	0.229
Don't look like myself	0(0.0)	9(100.0)	1(9.1)	10(90.9)	1.000
*Feeling nervous	4(50.0)	4(50.0)	2(18.2)	9(81.8)	0.319
Dry mouth	1(12.5)	7(87.5)	1(10.0)	9(90.0)	1.000
Hair loss	0(0.0)	17(100.0)	-	-	-
Additional 2	1(25.0)	3(75.0)	1(7.7)	12(92.3)	0.426
Shortness of breath	1(11.1)	8(88.9)	1(16.7)	5(83.3)	1.000
Change in taste of food	0(0.0)	2(100.0)	3(27.3)	8(72.7)	1.000
Constipation	1(100.0)	0(0.0)	4(33.3)	8(66.7)	0.385
Dizziness	2(33.3)	4(66.7)	4(57.1)	3(42.9)	0.592
Swelling of arms/legs	1(14.3)	6(85.7)	1(20.0)	4(80.0)	1.000
Sweats	2(25.0)	4(75.0)	1(33.3)	2(66.7)	1.000
Nausea	0(0.0)	3(100.0)	2(28.6)	5(71.4)	1.000
Problem with urination	-	-	0(0.0)	10(100.0)	-
Feeling drowsy	0(0.0)	5(100.0)	0(0.0)	2(100.0)	-

Feeling bloated	0(0.0)	1(100.0)	1(16.7)	5(83.3)	1.000
Difficulty swallowing	0(0.0)	3(100.0)	0(0.0)	3(100.0)	-
*Feeling irritable	2(66.7)	1(33.3)	0(0.0)	3(100.0)	0.400
Vomiting	0(0.0)	1(100.0)	1(25.0)	3(75.0)	1.000
Change in skin	0(0.0)	4(100.0)	0(0.0)	1(100.0)	-
Itching	2(66.7)	1(33.3)	1(50.0)	1(50.0)	1.000
Diarrhea	0(0.0)	1(100.0)	0(0.0)	2(100.0)	-
Problem with sexual interest/activity	1(100.0)	0(0.0)	0(0.0)	1(100.0)	1.000
Difficulty concentrating	1(100.0)	0(0.0)	-	-	-

-a: breast cancer patients were not assessed for relieve of problem with urination, so had 28 symptoms assessed for relieve

-b: gynaecological patients were not assessed for relieve of hair loss and difficulty in concentrating, so had 27 symptoms assessed for relieve.

\*: Psychological symptoms

The results of this study have shown the demographic distributions of the participants and comparisons made between the groups of patients. The effect of the educational status on the stage of disease and the duration of symptoms when the patients were interviewed were also highlighted. Peculiarities of gynaecological cancer patients with respect to treatment status in the study centre have also been brought to light as this differed from those of their breast cancer counter parts.

The average number of symptoms based on the MSAS-SF used in both groups of patients has shown comparable results and differences have also been highlighted. Both study groups also had additional symptoms outside the scope of the symptom assessment tool used and these symptoms were entirely different. When these optional symptoms were considered along with those of the MSAS-SF tool, the difference in the overall symptom prevalence between the two groups became significantly different both in quantity and quality.

Changes in symptoms in terms of relief or worsening of symptoms were assessed at an average of 9 days after the initial contact. There was generally poor symptom relief among the study participants. The next chapter discusses the implications and explanations of all of the findings in further detail.

## Chapter 5

### DISCUSSION

This cross-sectional prospective study was carried out in order to explore and compare symptom prevalence among gynaecological and breast cancer patients in a tertiary health care institution in North Central Nigeria. This study is the first Nigerian study to prospectively survey symptom prevalence among breast and gynaecological cancer patients as well as make comparison between these groups of patients in this institution.

#### Demographics

Breast cancer occurs in age groups that tend to differ more with race than with settings (64, 65, 170). Breast cancer is a postmenopausal disease among the whites in the developed countries but not so with blacks in the developing countries (43). A study by Bowen et al (170) reported an average age of 67 years among British white women while black Africa women have been shown to develop breast cancer in younger and premenopausal women with a significant number of them being in the active reproductive age group (1, 62,65). Anyanwu (43) in a ten year review of breast cancer in eastern Nigeria reported a mean age of 44 years and a peak age range of 35-39 years. Adesunkanmi et al (62) also in their study reported a mean age of 48 years. Both of these studies have reported lower mean ages for the breast cancer patients than the 52.78 years that was obtained in this study. The reported mean age in this study is however much lower than that reported by Bowen et al. The peak age of 40-49 years obtained in this study was also similar to that obtained among the 212 patients studied by Adesunkanmi. The reasons for the lower mean age obtained in those other studies could be because of the larger sample size in those retrospective studies compared to this study.

Patients with gynaecological cancers in this study were much older than the breast cancer patients. The mean age of 59.76 was slightly higher than 54 years reported by Nnadi et al (171) and 44.2 years reported by Kyari et al (172). Also apart from the larger sample sizes, these other studies encompassed a wider spectrum of gynaecological cancers which were not present in this study. The wide age ranges present in those studies were probably responsible for the lower

mean ages reported. The only three cancers captured in this study were cervical cancers, endometrial cancers and ovarian cancers. These other studies included choriocarcinoma, germ cell ovarian cancers, vaginal cancers, vulva cancers and fallopian tube cancers. These cancers incidentally were not seen during this study. Except for cervical cancer which occurs commonly in women of similar age group as that of breast cancers, at about 35-45 years, ovarian and most especially, endometrial cancers are essentially postmenopausal diseases (27). Over 40% of gynaecological cancers in this study were ovarian and endometrial cancer patients. This may explain the higher mean age and peak age obtained for gynaecological cancers in this study. This study also involved only adult female and as such, some ovarian cancer that are commonly found in children and adolescents were excluded. These other studies included these juvenile cancers and again, this may explain the lower mean ages reported compared to this study. The younger age of breast cancer patients compared to gynaecological patients could have implication for palliative or supportive care needs because of the effect of age on symptom experiences and distress. Younger patients with cancer tend to have more psychological problem than the older ones (173).

Breast cancer patients were more educated than the gynaecological cancer patients with 50% of them having at least a secondary school level of education compared to gynaecological patients with only a third of them having same level of education. The high proportion of breast cancer patients with at least a secondary school level of education was similar to 48.7% found in study by Adesunkanmi et al (62). This is not surprising since breast cancers occur in younger age than gynaecological cancers, and younger patients are more likely to be educated than the older ones because literacy level is gradually increasing in Nigeria, like in other developing countries (43).

#### Stage of Disease

The TNM staging is used commonly for breast cancers while the FIGO staging is commonly used in staging gynaecological cancer, but the TNM system for gynaecological cancers is also available and it is similar to the FIGO staging but with some subtle differences(174). Comparing breast and gynaecological cancers stage for stage is based on the general classification of stage 1 and 2 cancers as early cancers and stages 3 and 4 as late or advanced cancers (98,175). It is



acknowledged that the sub-classifications within each of the stages are of significant prognostic as well as therapeutic implications which may in turn affect symptom elaborations.

An advanced stage of disease at presentation to hospital, as was found in this study, is very common for many cancers in the developing countries (43,44), including cancers of the breast and cervix which are easily accessible organs for early detection of cancer (176). More than 80% of patients in both groups were at stage 3 or 4 of their disease based on their different systems of their tumour staging. This conforms to previous studies (1,2,43,74,78) in Africans that have shown that patients present in advanced stages of cancer.

The generally advanced stage of presentation of patients in this study was worse among the gynaecological cancer patients than the breast cancer patients in this study. One-fifth of breast cancer patients had early disease (stage 1 or 2) while only one-tenth of gynaecological cancer patients had stage 2 disease and none had stage 1 disease. The younger ages and the higher educational statuses among the breast cancer patients may have accounted for this little difference. When stages of diseases were compared with the educational status, patients with lower educational levels presented at more advanced stages of diseases than the educated patients. Some studies (2,77) in cancer patients have also reported more advanced stages of disease in patients with lower socio-economic class. However, among the educated patients, a higher proportion of those with tertiary level of education actually presented at more advanced stage disease compared to those with secondary level of education. This may imply that higher educational status does not result in early presentation to hospital. This was similar to the findings by Anyanwu (66) who reported similarly advanced stage of disease in their population of highly literate patients managed for breast cancer. Poor knowledge about cancer both by the educated and the uneducated people, even among health care providers have been reported by some authors (177). Attributing cancer to sorcery and witchcraft is believed by some people and this include both literates and illiterates (43,66). Cancer screening centre are also scarce in many African settings, including Nigeria (46) and the available once are poorly maintained and underutilized (2,59). All these contribute to late presentation of cancer cases to the hospital. Continuous public enlightenment by providing accurate information and embarking on awareness campaigns on cancer, training and retraining of health care providers, creating more

cancer screening centres as well as renovating the existing ones are needed in order to reduce the number of patients presenting in advanced stage of disease.

#### Duration of disease

The duration of disease in this study was based on time recollection by the patient. This may be affected by recall bias as individuals differ in their ability to correctly recall events. Patients with difficulties were aided by relating onset of disease with important festive periods and those on treatment were able to relate the duration on treatments to the duration of their disease. The duration of disease in both groups though appeared not to be significantly different, about 75% of gynaecological cancer patients were within 12 months of their disease compared to only 56% of breast cancer. By the third year of disease, fewer gynaecological patients were still accessing care compared to the breast cancer patients.

The median duration of symptoms of the disease at first interview had always been longer for breast cancer patients than for gynaecological cancer patients. Almost half (48.9%) of gynaecological cancer patients were seen within 6 months of onset of their disease while about a quarter (26.0%) of breast cancer patients were seen within the same period of time. This may be because gynaecological cancer patients experience more severe symptoms or more distressing symptoms compared to the breast cancer patients and these make them seek care earlier. It may also be that gynaecological cancers progress more rapidly than breast cancers, resulting in rapid deterioration in overall well-being, forcing them to seek care earlier. In contrast to short interval from cancer symptom occurrence to accessing care seen in gynaecological cancer patients, breast cancer patients had remained on treatment/follow up for longer periods of time than the gynaecological cancer patients. Forty-four percent of breast cancer patients were still accessing care more than a year after their first presentation to the hospital while only 24.5% of gynaecological cancer patients were still coming to access care. The main reason for this was because the breast cancer patients normally are prescribed hormonal therapy which is maintained for 5 years after the initial surgery and chemotherapy/radiotherapy. Treatment protocols in gynaecological cancers commonly do not normally involve such prolonged hormonal therapy.

Also, since gynaecological cancer patients were much older, there is the possibility of them dying from old age or other age related conditions than the younger breast cancer patients.

## Cancer treatment

Cancer treatment is a major problem in many African countries and this was also demonstrated in this study. Thirty percent of breast cancer patients in this study were not on anticancer treatment as at the time of first interview while over 90% of gynaecological patients also were not on any anticancer treatment. Among the breast cancer patients, financial constraints was the reason for none commencement of chemotherapy among 5 patients, 6 patients were experiencing delays before surgery while 4 patients were being managed for severe anaemia/respiratory distress and were yet to commence anticancer treatments. Gynaecological cancer patients are usually treated with surgery for operable cases and then have subsequent courses of chemotherapy or radiotherapy. Gynaecological cancers that are inoperable or that require additional therapy after initial surgery are referred for radiotherapy. Cervical cancer constituted more than 50% of the gynaecological patients in this study and many of them presented in advanced stage of disease for which radiotherapy referrals were made. Advanced stage at presentation for cervical cancers in the developing countries continues to occur in spite of cervical cancer being preventable through regular screening using papsmear or visual inspection of the cervix with acetic acid. The addition of Human Papilloma Virus vaccine to the preventive strategies in the recent past is expected to further reduce the incidence of cervical cancer (178). Screening for cervical cancer allows early detection of the disease at a stage when cure can be achieved and treatments are simple and affordable. Advanced cervical cancer requires chemoradiation in addition to complex cancer surgeries which are not readily available in many developing countries, including Nigeria (3,47)). Endometrial cancer patients are also usually referred for radiotherapy after initial debulking surgery. This very common referral of gynaecological cancer patients for radiotherapy outside the state may explain the fewer number of gynaecological patients still accessing care after one year of diagnosis. It is not always ascertained whether patients sent for further treatments like radiotherapy do report for such

intended therapy or not because funds are constantly a limiting factor in patients' management in this environment (60). As illustrated by Anyanwu et al in their study, many patients outrightly decline treatments while some that accept may not be able to continue due to cost as well as the inconveniences of travelling for radiotherapy outside their location of residence (66). Also contributing to fewer gynaecological cancer patients still accessing care long after their initial diagnosis is the fact that many patients do not report back for follow up even after completing the treatment for which they were referred. Other studies have also reported significant loss to follow up among cancer patients (62). The radiotherapy referral of gynaecological cancer patients is of great concern because there are very few number of radiotherapy machines in the country presently and they are not always in good functional states (2) yet patients are being referred continuously because that is the only feasible anticancer treatment for some patients. It is not known if these referred patients actually ever get to their destination or even receive the prescribed radiotherapy. This problem with radiotherapy referral was demonstrated in this study as more than 20% of gynaecological cancer patients were already referred but all were yet to go for financial reasons as well as lack of information on the functionality of the radiotherapy centers. The nearest radiotherapy facility to the study facility is about 3 hours drive away and it was not functioning at the time of this study. The other radiotherapy facilities were much further away and there was no ready information on their functionality. Another 30% of gynaecological cancer patients were still being evaluated at the time of the study; all were cervical cancer patients and were likely to end up being referred for radiotherapy as well. All the three gynaecological cancer patients that had received radiotherapy in this study all had cervical cancer and all were referred to the palliative care team by their primary physicians because there were no further anticancer treatments available for them. Their palliative care referral was indicative of the palliative intent of the radiotherapy treatment they had received.

### Symptom Prevalence

The prevalence of symptoms in this study ranged from 0 – 18. This was lower than a range of 0 - 25 reported by Portenoy et al(179) but comparable to 1 -18 symptoms reported by Tsai et al(180) both of which were studies conducted in similar cancer population to this study. About 20% of patients in this study had 0 or 1 symptom only. The heterogeneity of patients in terms of stages of disease and treatment statuses could explain the widely differing symptom prevalence.

The overall mean number of symptoms was based on the symptom assessment tool used with limited availability for inclusion of additional symptoms not enlisted in the tool. The overall mean number of symptoms was  $6.9 \pm 4.7$  and the median was 7 symptoms in this study. The result is comparable with that obtained for a cancer population studied in London (129) but it was much lower than that reported in a similar group of patients studied in Africa (6).

Considering the additional symptoms was important in this study because some patients, especially the gynaecological cancer patients had none of the 32 symptoms listed in the MSAS-SF tool and the additional symptoms were the only symptoms documented for them. Such gynaecological cancer patients had only vaginal bleeding and foul smelling vaginal discharge as their only symptoms. In considering the additional symptoms, the mean number of symptom for breast cancer patients was 5.8 and that of gynaecological cancer patients was 8.1. This difference in the mean number of symptoms was significantly different between the two groups of patient with the gynaecological cancer patients having more symptoms which can be attributed to additional symptoms not listed in the MSAS tool. These mean numbers of symptoms were much lower than  $18 \pm 6.6$  reported by Harding et al (6) and also  $10.2 \pm 5.8$  reported by Lidston et al (181). It was however slightly higher than the overall mean of 5 symptoms reported by Potter et al (120). Harding et al (6) study was conducted in patients already referred for palliative care intervention, signifying advanced cancer in all of their patients, and this alone may explain the higher mean number of symptoms. Also, patients with HIV infection also constituted a significant proportion of Harding et al study population and this also may explain the higher number of symptoms in their study population. HIV infection itself is associated with significant psychological and physical symptoms due to its multi-systemic effects (149). Although HIV was not the focus in this study, three of the patients had HIV infection documented in their case notes. But these three are much lower in comparison to the number of HIV infected patients in Harding's study. The lower mean number of symptoms obtained in this study compared to that of Harding et al (6) may also be due to additional symptoms which were eight in number, incorporated into the MSAS-SF used in that study compared the optional one or two additional symptoms that was added if present in this study.

The study by Lidston et al (181) was a mixture of both early and advanced cancer patients attending clinics at a cancer center and this was similar to this study population in this regard. The lower mean number of symptoms obtained in this study compared to that of Lidston et al

(181) could be explained by the other cancer sites that were represented in that study. These included lung, brain, head/neck and gastrointestinal cancers in addition to breast and gynaecological cancers. Lung and brain cancers had the highest number of symptoms in that study, followed by breast, gastrointestinal and head/neck cancers. Gynaecological cancers were among cancers with the least number of symptoms in Lidston's study.

The patients in Potter et al (120) study were freshly referred to palliative care services and just over 70% of them had advanced cancer, making it comparable to this study population in whom about 80% of them also had advanced cancer. Potter's study consisted of patients that were seen in 4 different settings. Those in the outpatient and inpatient settings actually had lower mean number of symptoms of 3.3 and 2.7 respectively. Patients seen at the hospice and community service points had higher mean number of symptoms of about seven. Comparing the outpatient and hospital inpatients that were of similar setting to this study population, the mean number of symptoms in Potter's study was much lower than that obtained in this study. It is possible that the retrospective nature of Potter's study with the high probability of under-reporting and under-documentation of symptoms may have accounted for this lower symptom prevalence.

The overall ten most frequent symptoms in this study were pain, weight loss, worrying, feeling sad, lack of energy, difficulty in sleeping, lack of appetite, numbness/tingling in hand and feet, 'don't look like myself, and cough. Comparing these with the top 10 most prevalent symptoms in a systematic review by Kim et al (94) and Reily et al (182), 6-8 of these symptoms were replicated in this study. Also, Teunissen et al's (95) top five symptoms of fatigue, pain, lack of appetite, weakness and anorexia are similarly found in this study. The symptoms reported in this study correlated well with finding from other studies that have used similar symptom assessment tool.

#### Common symptoms in this study

The top 5 most prevalent symptoms between the two study groups were similar but different in sequence. For breast cancer patients, pain, worrying, feeling sad, weight loss and difficulty sleeping were the top 5 symptoms. The top 5 symptoms for gynaecological cancer patients were weight loss, pain, worrying, feeling sad and lack of appetite. Four of these top five symptoms that were common to both study groups occurred in higher frequencies among the

gynaecological patients. Both the gynaecological cancer patients and breast cancer patients reported pain and weight loss as the most common physical symptoms while feeling sad and worrying were the two most prevalent psychological symptoms reported. Similar symptom prevalence studies on breast and gynaecological cancer patients by Aeckerle et al in Germany (108) reported on weakness, pain and anorexia as the most common symptoms in their study population of 225 patients. Other notable symptoms in Aeckerle et al's (108) study were dyspnoea, nausea/vomiting. The symptoms reported by Aeckerle et al's (108) study were mainly physical symptoms extracted from medical records and this may explain the limited number of symptoms as well as the absence of psychological symptoms. A similar study in Ibadan, Nigeria (109) reported on pain, vomiting, nausea, weight loss and lymphedema as the top 5 and similarly prevalent symptoms in breast and cervical cancer patients. Here again, the study was retrospective in nature and symptoms reported on were just the symptoms documented in the medical records and psychological symptoms were absent. Studies have shown that psychological symptoms are commonly overlooked in patients with advanced cancer (183). This study has shown that with the use of a symptom assessment tool that ensures questioning about psychological symptoms, they have been shown to be quite prevalent. Almost all of the patients had been under the care of their attending physicians for several weeks/months before being recruited for this study. All had clinical diagnosis of cancer, some were currently on treatments, some had completed available anticancer treatments, others were awaiting commencement of treatments and some were being referred for radiotherapy. Forty percent of the top most common symptom in this study was psychological symptoms, yet none of the patients had any psychological nor psychiatrist referral or evaluation. Only 11% of the patients had palliative care referral. This shows that psychological symptoms assessment needs to be incorporated into the evaluation of breast and gynaecological cancer patients in this hospital. Many oncologists agree that palliative care should be incorporated into comprehensive cancer care at the point of diagnosis, many also claim to be rendering palliative care already, but evidence show that it is either not done at all or it is inadequately done (184). This is an important information for the primary physicians in this hospital who most of the time manage these cancer patients alone without the involvement of the palliative care team or psychiatrist/psychologists.

This study revealed that breast and gynaecological cancer patients significantly differed with respect to certain symptoms. Gynaecological cancer patients had higher frequencies of symptoms

that are related to gastrointestinal and urinary systems compared to breast cancer patients. The proximity of the gynaecological organs to these systems may account for many of the symptoms. Breast cancer patients conversely had chest symptoms such as cough and shortness of breaths more commonly than in the gynaecological cancer patients. These findings are similar to that reported by Lidston et al in their study. Although not statistically significant, gynaecological cancer patients had higher frequency of psychological symptoms than the breast cancer patients. This contrasts the finding in other studies that have reported higher occurrence of depressive symptoms among breast cancer patients compared with gynaecological cancer patients (181,183). Also in contrast to findings in other studies that have reported higher frequency of psychological symptoms in younger age women (173), breast cancer patients in this study were younger than the gynaecological patients, yet, psychological symptoms were more in the gynaecology than the breast cancer patients. While this may be a genuine finding in our environment, the fact that many of the gynaecological cancer patients were inpatients, had higher frequencies of the presence of additional symptoms and also had worse performance status scores may explain this higher frequency of psychological symptoms in them. More than two-thirds of the gynaecological cancer patients had notable additional symptoms that were not captured in the 32 symptoms listed in the MSAS-SF. In contrast to this observation, only one-third of breast cancer patients had additional symptoms not already listed in the MSAS-SF. Breast cancer patients had hair loss exclusively in them. This reason for this was because many of them were on chemotherapy while gynaecological patients were either awaiting or had completed chemotherapy at the time of the study. The symptom list in the MSAS-SF seems to adequately cover chemotherapy induced symptoms. This finding in this study shows that the present symptom list in MSAS tool may be adequate for symptom assessment in breast cancer patients for this environment but may require modifications in order to adequately accommodate gynaecological cancer patients' symptom profiles. The symptoms for which breast and gynaecological patients significantly differed in this study are noteworthy for palliative care team who see all cancer patients of different diagnoses. The palliative care team is usually called in to co-manage patients with uncontrolled pain in this hospital. The reported symptoms from this study represent additional symptoms that the palliative care team could enquire about, pending the availability and acceptability of an assessment tool in the routine care of patients in this hospital. This prior knowledge of the common symptoms of these groups of cancer will help to



guide patients' management and inform other supportive measures that will help to improve care and quality of life for the patients.

### Most Distressing symptoms

The multidimensional measurement of symptoms made possible by the use of MSAS makes it easy to be able to identify the most distressing symptoms in the list of symptoms while the MSAS subscales also helps to categorize the type of distress by assessing the scores obtained from a constellation of some specific symptoms. The mean GDI, MSAS-PHYS, MSAS-PSYCH and TMSAS in this study were all low compared to other studies assessing these scales. The mean GDI of  $0.76 + 0.68$  obtained in this study was much lower than 1.61 and 1.74 obtained by Richard et al(149) and Harding et al(6) in their studies and still lower than 1.3 reported by Portenoy et al(179). The study by Harding et al involved HIV positive patients already committed to palliative care while the second study, although done on cancer patients had one-fifth of the study population having HIV diagnosis unlike this study where only 3% had HIV diagnosis. Both of Harding's studies were conducted in patient populations in the palliative care settings, signifying advanced diseases in all of the patients. This may explain the higher GDI scores in these studies compared to my study. Portenoy's study was done on cancer population similar to this study with respect to inpatients and outpatients at various cancer stages in a hospital setting and not necessarily palliative care setting. The higher GDI in Portenoy's study also may be due to wider cancer populations involving colon and prostate cancer and the fact that over 60% of that study population was those with metastatic disease (stage 4) unlike this study where only 20% of the study population had stage 4 diseases. It may also indicate that current management is taking care of most of these symptoms and that specialist palliative care referral is not necessary.

Similarly, the mean scores for MSAS-PHYS of  $0.58 + 0.6$  and MSAS-PSYCH of  $0.75 + 0.78$  reported in this study were also much lower compared to the above studies that have reported on these MSAS sub-scale scores. Again, the HIV status, the palliative care settings and the higher proportion of patients with metastatic diseases as earlier highlighted may explain the higher scores ranging between 0.9 – 1.48 for MSAS-PHYS and 1.1 – 1.56 for MSAS-PSYCH reported in the above mentioned studies.

This study however revealed differences in the two study groups. The MSAS-PHY and the GDI show that the gynaecological cancer patients were both physically and globally more distressed than their counterpart breast cancer patients. Again, this may probably be a reflection of the higher frequency of symptoms in them. The Karnofsky Performance Score which is also closely related to the presence of symptoms was also lower in the gynaecological patients, implying possibly more distress in the gynaecology patients. The most distressing symptoms for breast cancer patients were feeling bloated, vomiting; don't look like myself and pain. Other symptoms rated as most distressing were not listed in the MSAS tool and included presence of fungating breast masses, neck swelling and immobility. Gynaecological cancer patients similarly had body image issue and pain as most distressing as in the breast cancer patients but also in addition, had problems with urination, difficulty sleeping, vulva swelling, vaginal bleeding, vaginal discharge, abdominal swelling and abnormal posturing as most distressing too. "Don't look like myself" which connote a body image issue and pain were the two symptoms that cut across this study population as most distressing. Pain has similarly been reported in many studies to be very distressing and results in aggravation of other symptoms. Any mutilating surgery is also likely to result in a sense of poor body image in any patient. For the breast cancer patients in this study, mastectomy and the presence of huge fungating breast masses constituted disfigurement which resulted in poor body image in these patients. Among the gynaecological patients, weight loss and body swellings were the reasons for poor body image. A sense of poor body image negatively affects sexuality and sexual function (185,186). For many women, the breast is considered an important component of womanhood and loss of it negatively affects the physical appearance as well as the psyche of most women (186,187). Chemotherapy also contributes to reduction of sexual function by inducing menopause or worsening menopausal symptoms for those that are already menopausal (185). Gynaecological cancer survivors in developed countries commonly encounter post treatment sexual dysfunction arising from surgical procedures or pelvic radiotherapy (185). The reasons for sexual dysfunction in this environment are quite different because of late presentation of cancer which commonly precludes such extensive surgical interventions as well as poor accessibility and affordability of radiotherapy facilities. Nearly half of the gynaecological cancer patients in this study were having vaginal bleeding and or foul vaginal discharge which in themselves were impediments to sexual relations. The only three gynaecological cancer patients that had received radiotherapy were severally ill from their

cancers were all referred to palliative care team for end-of-life care. Although almost all the patients in this study claimed not to have any problem with sexual relation or interest as it was stated in the MSAS-SF, majority of them actually do not consider sexual relationship a priority in their present predicaments of battling with cancer diagnosis. Despite asking with much sensitivity and caution, some of them were still offended and other embarrassed by the questioning. It may be more appropriate to find ways to identify patients that will be willing to discuss sexual issues and who may then require advice in this regards other than asking very patient this sensitive question. This is especially so in this environment where sexual issues are not commonly discussed openly (188).

All the psychological symptoms were not considered distressing by both gynaecological and breast cancer patients and there was no difference between the two groups with respect to the psychological MSAS subscale (MSAS-PSYCH). The low distress caused by the psychological symptoms may be responsible for the non-treatment in spite of the high prevalence. The possibility of under-reporting of the distress caused by psychological symptoms may be due to more focus on physical symptoms, especially if they are severe. The low scores for psychological symptoms reported in this study may also be attributed to poor understanding of cancer as a disease among the populace (189,190). Other studies have highlighted that poor cancer knowledge is common to both literates and the non literates (54)(66). Among the literates and those with the knowledge of the life threatening nature of cancer, the influences of culture and religion may tend to override the knowledge (191,192) and this may account for the low level of psychological distress reported in this study. The high prevalence of psychological symptom though with low level of distress is a pointer to the need for repeated or close psychological monitoring as the disease progresses or as the patients understand their illness better.

### Symptom Relief

Symptom relief in this study was assessed by an average of 8 days after the initial interview. The heterogenous cancer stages and treatment statuses was a possible bias to this assessment. Also, the average of 8 days interval between the assessments may be too short, especially for those that were yet to commence treatment.

Relief of symptoms was not different between the breast and gynaecological cancer patients in physical symptoms that were common to both groups. The breast cancer patients were assessed for relief of 28 physical symptoms but relief was noted for only 4 symptoms- constipation, itching, problem with sexual interest and difficulty in concentration. Gynaecological cancer patients were assessed for relief in 27 physical symptoms and relief was documented for only two symptoms which are dizziness and itching. Generally, more symptoms were relieved among the breast cancer patients than the gynaecological patients. Pain was the most prevalent symptom in this study with a rate of 63.6%, and pain relief was reported in only one-third of the patients with the complaint of pain. Although pain management is almost the only major reason for palliative care referral in this hospital, not all patients with pain were referred. While it is not only palliative care providers that can manage pain, they are more likely to do it better than physicians without palliative care experience. This is because palliative care providers holistically approach symptom management in life threatening diseases and are more likely to treat pain using the concept of total pain.

Psychological symptoms though not considered to be significantly distressing, were also poorly improved among the study population. All the psychological symptoms of feeling sad, worrying, feeling irritable and feeling nervous were not improved at second contact in majority of gynaecological cancer patients (73.9-100%). Breast cancer patients also had at least half of them not relieved of feeling sad, worrying and feeling nervous. Feeling irritable was much improved among the breast cancer patients at the second contact. This study has shown high prevalence of psychological symptoms which did not improve overtime. This further emphasizes the need for psychological assessments and interventions in addition to the present routine care being offered to breast and gynaecological cancer patients in this center. It is only a holistic approach to care that can bridge this gap. The holistic approach is the hallmark of palliative care and was shown to be lacking in the care of majority of these patients. Referral for a palliative care consultation for this study population was generally poor considering the advanced stage of disease in most of the patients as well as the high prevalence of symptoms reported in this study. The present practice in this hospital is for the palliative care team to be invited to help co-manage poorly controlled pain only and occasionally and at the discretion of the managing physicians, and also to help co-manage patients at the end-of life. The fact that cancer patients have life-threatening conditions for which palliative care needs to be applied right from the point of diagnosis and

along with active anticancer treatments is not yet well appreciated by many physicians in this hospital. As at the time of this study, only 6% of breast cancer patients and 16% of gynaecological cancer patients had palliative care referral evident in their case notes. More gynaecological cancer patients were referred for palliative care than the breast cancer patients, probably because of inpatient status that was commoner with the gynaecology patients and also the poorer performance levels of these patients as was earlier mentioned.

## Conclusion

This study has shown that breast and gynaecological cancer patients in this hospital do have significant symptoms that are poorly addressed. The paucity of funds to commence and maintain treatments and outright non availability of some other anti-cancer treatments all contribute to disease progressions and worsening of symptom burden. These are pointers to the need for palliative care in the majority of patients accessing care in this hospital. The poor relief of symptoms noted in this study is therefore not unexpected. If this trend continues, it will pave way for patients' and their families' dissatisfaction with the health care services and it will lead to distrust of the health care systems, which further pushes patients away from seeking care early. A possible way of forestalling this situation is to integrate palliative care into the care of these patients at every available service point and early in the course of their disease. Studies (159,193, 194) have shown that palliative care involvements in patients' care improve symptoms control and also patients' and their families' satisfaction. These interventions have been shown to be effective in various settings including hospital-based inpatient care (193), home-based care (196), community settings as well as outpatient settings (120). There is the need for the primary physicians attending to cancer patients to be trained in palliative care. This would improve their understanding of palliative care so that they can also implement palliative care earlier and also refer for specialist palliative care services when necessary. Advocacy for patients to be referred for palliative care is the right thing to do, but the limited availability of palliative care specialists in the country is also well known (197). The present palliative care team in the hospital has limited capacity to cater for the load of patients requiring palliative care. An interim solution will be for the primary physicians to be trained in general palliative care pending the widespread availability of specialist palliative care providers.

### Limitation of the study

This study was a hospital based study and as such the findings may not be generalized to the whole community.

Symptom assessment as well as its relief was assessed across board and the patients varied in stage of diseases and treatment status with some having completed anti-cancer treatment while some were currently on treatment and others were yet to commence treatments. The varied stages of diseases and treatment status within and between the studied groups may have had an effect on symptom prevalence and actual relief as well as perception of relief in some patients. Also, treatment interventions could not be assessed in detail because it was not known if the patients mentioned their symptoms to their attending physicians.

The 8 days interval for symptom re-assessment was also short, especially for patients that were yet to commence anti-cancer treatment

## CHAPTER 6

### CONCLUSIONS AND RECOMMENDATIONS

#### CONCLUSIONS

The aim of this study was to assess and compare the prevalence and burden of symptoms among breast and gynaecological cancer patients accessing care at the University of Ilorin Teaching hospital, Ilorin, Nigeria. This was accomplished with the aid of a symptom assessment tool, the MSAS-SF. The objectives of the study were to determine the most prevalent symptoms, the most distressing symptoms as well as assess symptom relief among the two groups of patients. The performance status of the patients were also assessed and compared between the groups of patients.

Both the breast and gynaecology cancer patients described pain, weight loss, worrying and feeling sad as the top 4 symptoms similarly in them albeit of different order. Fifty percent of these were psychological symptoms (worrying and feeling sad) while the remaining 50% were physical symptoms (pain and weight loss). This further reaffirms the high prevalence of psychological symptoms and that it may be as important as physical symptoms in cancer patients.

The finding shows higher symptom prevalence among the gynaecological cancer patients than the breast cancer patients. Gynaecological patients also had higher frequencies of urinary and gastrointestinal symptoms than breast cancer patients who also in turn had higher frequency of chest symptoms such as breathlessness and cough more frequently than the gynaecology patients.

Comparatively, gynaecology patients were more globally (GDI) and physically (MSAS-PHYS) distressed than the breast cancer patients. However, both groups were comparable with respect to psychological distress (MSAS- PSYCH).

Although the study was not interventional as patients received routine care from their managing physicians, there was poor relief of symptoms among majority of the patients studied.

This study have shown that breast and gynaecological cancer patients do have significant physical and psychological symptoms, some of which are quite distressing and the relief of many of the symptoms were equally suboptimal. This shows an unmet need for symptom assessment as well as symptom control in these groups of patients.

## RECOMMENDATIONS

Advanced stage of disease at presentation in majority of the patients in this study is a reflection of poor knowledge about cancer in many of the patients and also poor cancer screening services that can help detect early stage diseases that are simpler and less costly to manage. This is a call to action for all those responsible for cancer care and control to further intensify or develop other strategies that would result in prevention and early detection of cancers.

The study revealed a high symptom prevalence, poor symptom relief as well as poor palliative care referral of breast and gynaecological cancer patients. It has been advocated that palliative care should be introduced early in the course of cancer care, but this becomes more imperative for those presenting in advanced disease for which treatment intent is palliative right from the point of diagnosis. The infrequent palliative care referral by the managing physicians in this study points to poor knowledge and understanding of palliative care among health care providers currently managing these patients. It is recommended that the physicians managing these patients should be educated on palliative care so that they can learn to introduce such care early in the course of managing their patients. This is also a recommendation of the World Health Assembly Resolution on strengthening palliative care as a component of comprehensive care throughout the life course which states that intermediate training in palliative care “should be offered to all health care workers who routinely work with patients with life-threatening illnesses, including those working in oncology” (198).

It is suggested that protocols are developed to help guide the physicians as to when to consider palliative care involvement in both early and late staged cancer patients since the transition from curative treatment to palliative treatment is not always clear cut.



Poor symptom assessment and subsequent poor symptom relief as shown in this study indicates need for adequate symptom assessment. It is recommended that the clinics should adopt any of the available validated symptom assessment tools or develop their own tool to capture the common symptoms peculiar to their cancer sub-populations. The development of cancer site-specific symptom assessment tool is particularly more relevant for gynaecological cancer patients in this environment because this study has shown that gynaecological cancer patients had significant symptoms that were not enlisted in the symptom assessment tool that was adopted for this study. It is also recommended that the validated tools available now such as ESAS, MDASI and MSAS should also be validated in Nigeria for possible adoption in managing cancer patients.

The adoption of a symptom assessment tool in itself is not enough because its implementation is equally important. The crowded and multi-specialist clinics' running simultaneously as it is presently the case may make implementation very difficult. There is therefore the need to also train other clinic staff especially the nurses that organize the clinics, on the use and need for the symptom assessment tool to be adopted. There is also the need for patients to be educated on the use and benefits of the tool in order to encourage acceptance on the part of the patients.

Further studies on how best to implement a symptom assessment tool in typical busy hospitals that characterize many developing countries like Nigeria is highly needed.

This study has also highlighted the high prevalence of psychological symptoms which were not assessed nor relieved. This also calls for re-education of the managing physicians on the need for routine psychological assessment or screening of cancer patients. Such screening will allow involvement of psychologist or psychiatrist either alone or in conjunction with a palliative care team in the care of patients needing such specialist care.

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## APPENDIX I

**Information Sheet for:**

*An Exploration of symptom burden among breast and gynaecological cancer patients accessing care at the University of Ilorin Teaching Hospital.*

Thank you for giving your time to hear about our research study.

This information sheet tells you about a research study that you may wish to take part in. You may have some further questions to help you decide whether you want to take part. You can ask any further questions from your clinical team, from the researcher, or using the telephone numbers at the end.

Thank you for thinking about whether you want to take part. Please take your time to make a decision.

**What is the purpose of the study?**

We are looking at the symptoms experienced by breast cancer and gynaecological cancer patients and checking if these symptoms are well noted and being treated by the attending doctors.

**Do I have to take part?**

No, you don't have to take part. If you do agree to take part, you are free to withdraw from the interview at any time without giving us any reason. Whether or not you take part, your care will NOT be affected in ANY WAY. If you do agree to take part, you will be asked to sign a consent form, which shows that you have agreed to do so. You can take some time to think about whether you would like to take part, and you may want to talk it over with your family, friends or someone in your care team.

**What will happen if I take part?**



An experienced researcher will speak to you and ask you questions about you and your health, and this may include any pain or other problems you have and how well they are being controlled. It will take around 15-20 minutes for the interview. We will need to check your hospital case notes for further information on your disease and the treatment your doctors have planned for you or that they are already giving you. This will take 10-20 minutes and we may check your case note before speaking to you or vice versa. The checking of the case note is not part of the time we need to spend with you. This information sheet is for you to keep.

### **Benefits of the study**

There are no direct benefits to the study for participants although people who have been interviewed using these questionnaires find that they are good points for discussion with care providers. The anticipated benefits are in identifying people's care needs and in trying to meet those needs.

### **What are the risks of the study?**

There are few study risks. Answering some questions might cause an emotional response. The researchers and counselors are trained to assist if the questions cause an emotional response. The researcher will stop the study and ask you if you would like assistance

### **Will my taking part in this study be kept confidential?**

All the information which we collect during the interview will be kept strictly confidential. You will not be identified in any way, and your personal details (for example name and address) will be kept separately from the information you give. We will use a number and not your name on any information you give us. No-one outside the study will have access to the information you give us.

For patients in this study we will record their illness. That information will be treated as confidentially as all the other information you give us, and no-one outside this study will be able to find out your name or any other information that would identify you.

### **How will I know about the results of the study?**

At the end of the study a report will be sent to the clinic/outpatient department and to the people who took part in the study.

**Who is organising the research?**

If you need to talk to someone about this research, you can contact the this person:

Dr Isiaka-Lawal Salamat, Kwara State Specialist Hospital, Sobi, Ilorin.

08039124662.

**APPENDIX II**

**Consent form for: an exploration of symptom burden among breast and gynaecological cancer patients accessing care at UITH, Ilorin**

1. I confirm that I have read and understand the information sheet and have had the opportunity to ask questions.
2. I understand that my participation is voluntary and I am free to withdraw at any time, without giving a reason, without my care being affected.
3. I agree to take part in the above study.

Name \_\_\_\_\_

Signature \_\_\_\_\_

Date \_\_\_\_\_

Researcher: Signature \_\_\_\_\_

Date: \_\_\_\_\_

Witness: Name

(from clinical team or family member)

Signature \_\_\_\_\_

Date: \_\_\_\_\_

**APPENDIX III**

Study ID N0\_\_\_\_\_Date 1<sup>st</sup> Contact \_\_\_/\_\_\_/\_\_\_ Proposed 2<sup>nd</sup> Contact\_\_\_/\_\_\_/\_\_\_ Phone\_\_\_\_\_

**MEMORIAL SYMPTOM ASSESSMENT SCALE – Short Form [MSAS-SF]**

- I. INSTRUCTIONS: Below is a list of symptoms. If you had the symptom DURING THE PAST WEEK, please check Yes. If you did have the symptom, please check the box that tells us how much the symptom DISTRESSED or BOTHERED you.

<p>Check <u>all</u> the symptoms you have had during the <b>PAST WEEK.</b></p>	<b>→→ IF YES: How much did it DISTRESS or BOTHER you?</b>					
	<b>Yes</b>	<b>Not at</b>	<b>A little</b>	<b>Some-</b>	<b>Quite</b>	<b>Very</b>
	[✓]	<b>All</b> [0.8]	<b>Bit</b> [1.6]	<b>what</b> [2.4]	<b>a Bit</b> [3.2]	<b>Much</b> [4.0]

<b>Difficulty concentrating</b>					
<b>Pain</b>					
<b>Lack of energy</b>					
<b>Cough</b>					
<b>Changes in skin</b>					
<b>Dry mouth</b>					
<b>Nausea</b>					
<b>Feeling drowsy</b>					
<b>Numbness/tingling in hands and feet</b>					
<b>Difficulty sleeping</b>					
<b>Feeling bloated</b>					
<b>Problems with urination</b>					
<b>Vomiting</b>					
<b>Shortness of breath</b>					
<b>Diarrhea</b>					
<b>Sweats</b>					
<b>Mouth sores</b>					
<b>Problems with sexual interest or activity</b>					

Itching					
Lack of appetite					
Dizziness					
Difficulty swallowing					
Change in the way food tastes					
Weight loss					

**MEMORIAL SYMPTOM ASSESSMENT SCALE – Short Form [MSAS-SF]**

I. INSTRUCTIONS: Below is a list of symptoms. If you had the symptom DURING THE PAST WEEK, please check Yes. If you did have the symptom, please check the box that tells us how much the symptom DISTRESSED or BOTHERED you.

<p>Check <u>all</u> the symptoms you have had during the <b>PAST WEEK</b>.</p>	<p><b>→→ IF YES: How much did it DISTRESS or BOTHER you?</b></p>					
	<p>Yes</p> <p>[✓]</p>	<p>Not at</p> <p>All</p> <p>[0.8]</p>	<p>A little</p> <p>Bit</p> <p>[1.6]</p>	<p>Some-</p> <p>what</p> <p>[2.4]</p>	<p>Quite</p> <p>a Bit</p> <p>[3.2]</p>	<p>Very</p> <p>Much</p> <p>[4]</p>

Hair loss					
Constipation					
Swelling of arms or legs					
“I don’t look like myself”					
<p><b>If you had <u>any other symptoms</u> during the PAST WEEK, please list them below, and indicate how much the symptom DISTRESSED or BOTHERED you.</b></p> <p>1. _____</p>					
<p>2. _____</p>					

II. Below are other commonly listed symptoms. Please indicate if you have had the symptom DURING THE PAST WEEK, and if so, how OFTEN it occurred.

Check <u>all</u> the symptoms you have had during the PAST WEEK	→ → IF YES, How OFTEN did it occur?				
	Yes	Rarely	Occasionally	Frequently	Almost
	Constantly				
	[✓]	[1]	[2]	[3]	[4]
Feeling sad					
Worrying					
Feeling irritable					
Feeling nervous					



## Memorial Symptom Assessment Scale Subscales

The scoring of the MSAS yields several validated subscale scores.

A 10 item MSAS **Global Distress Index** (MSAS-GDI) is considered to be a measure of overall symptom distress. The GDI is the average of the frequency of 4 prevalent psychological symptoms (feeling sad, worrying, feeling irritable, and feeling nervous) and the distress associated with 6 prevalent physical symptoms (lack of appetite, lack of energy, pain, feeling drowsy, constipation, dry mouth).

The **Physical Symptom Subscale** score (MSAS-PHYS) is the average of the frequency, severity and distress associated with 12 prevalent physical symptoms: lack of appetite, lack of energy, pain, feeling drowsy, constipation, dry mouth, nausea, vomiting, change in taste, weight loss, feeling bloated, and dizziness.

The **Psychological Symptom Subscale** score (MSAS-PSYCH) is the average of the frequency, severity and distress associated with 6 prevalent psychological symptoms: worrying, feeling sad, feeling nervous, difficulty sleeping, feeling irritable, and difficulty concentrating.

The **Total MSAS score** (TMSAS) is the average of the symptom scores of all 32 symptoms in the MSAS instrument. Each symptom score is an average of its dimensions.

In the short form, there is only one dimension for each symptom, distress for physical symptoms and frequency for psychological symptoms.

## Memorial Symptom Assessment Scale Short Form Subscales

The scoring of the MSAS-SF yields several validated subscale scores.

A 10 item MSAS **Global Distress Index** (MSAS-GDI) is considered to be a measure of overall symptom distress. The **GDI** is the average of the frequency of 4 prevalent psychological symptoms (feeling sad, worrying, feeling irritable, and feeling nervous) and the distress associated with 6 prevalent physical symptoms (lack of appetite, lack of energy, pain, feeling drowsy, constipation, dry mouth).

$MSAS\ SF\ GDI = (\text{feeling sad, worrying, feeling irritable, feeling nervous, lack of appetite, lack of energy, pain, feeling drowsy, constipation, dry mouth})/10$

The **Physical Symptom Subscale** score (MSAS-PHYS) is the average of the distress associated with 12 prevalent physical symptoms: lack of appetite, lack of energy, pain, feeling drowsy, constipation, dry mouth, nausea, vomiting, change in taste, weight loss, feeling bloated, and dizziness. Note that the scaling is in increments of 0.8, with zero for no symptom, 0.8 for symptom present but no distress, and upwards for increasing levels of distress.

$MSAS\ SF\ PHYS = (\text{lack of appetite, lack of energy, pain, feeling drowsy, constipation, dry mouth, nausea, vomiting, change in taste, weight loss, feeling bloated, and dizziness}) / 12$

The **Psychological Symptom Subscale** score (MSAS-PSYCH) is the average of the frequency associated with 6 prevalent psychological symptoms: worrying, feeling sad, feeling nervous, difficulty sleeping, feeling irritable, and difficulty concentrating. Scoring is in increments of one, with zero for no symptom to 4 for “almost constantly”.

$MSAS\ SF\ PSYCH = (\text{worrying, feeling sad, feeling nervous, difficulty sleeping, feeling irritable, and difficulty concentrating})/6$

The **Total MSAS score** (TMSAS) is the average of the symptom scores of all 32 symptoms in the MSAS instrument.

In the short form, there is only one dimension for each symptom, distress for physical symptoms and frequency for psychological symptoms. The sequence of symptoms in the short form is different from that in the long form.

Scoring of physical symptoms in the MSAS-SF is as follows:

- Zero if the symptom is not present
- 0.8 if the symptom is present but causes no distress
- 1.6 if the symptom is present and causes a little bit of distress
- 2.4 if the symptom is present and causes somewhat of distress
- 3.2 if the symptom is present and causes quite a bit of distress
- 4.0 if the symptom is present and causes very much distress.

Scoring of psychological symptoms is:

- 0 if the symptom is absent
- 1 if the symptom is present and occurs rarely
- 2 if the symptom is present and occurs occasionally
- 3 if the symptom is present and occurs frequently
- 4 if the symptom is present and occurs almost constantly.

**APPENDIX IV**

Participant Data Sheet

Date : \_\_\_\_\_ Where seen: \_\_\_\_\_ Study NO \_\_\_\_\_ Phone  
NO \_\_\_\_\_

Age: \_\_\_\_\_ Occupation \_\_\_\_\_

Educational level: a) None b) primary c) secondary d) tertiary

Religion: \_\_\_\_\_

Ethnicity: a) Yoruba b) Hausa c) Igbo d) Others \_\_\_\_\_

Duration of illness: \_\_\_\_\_

Diagnosis: \_\_\_\_\_ Diagnosis confirmed by histology: Yes( ) No( )

Stage documented: \_\_\_\_\_ Stage not documented: ( ) Tick

Indication for present admission (inpatients  
only): \_\_\_\_\_

Previous cancer specific treatment (if applicable): Tick all that apply.

- i. Chemotherapy
- ii. Surgery
- iii. Radiotherapy
- iv. Hormonal therapy
- v. None

Current cancer specific treatment: \_\_\_\_\_

Number of Courses of treatment (Chemotherapy/Radiotherapy) \_\_\_\_\_

Status of treatment : Ongoing/ Abandoned/Completed/Interrupted/Others  
(specify) \_\_\_\_\_

Remarks \_\_\_\_\_  
\_\_\_\_\_

Involvement of hospital palliative care unit in management: Yes/No

Present drug management (both cancer specific and non-cancer specific)

- |          |          |
|----------|----------|
| 1. _____ | 5. _____ |
| 2. ----- | 6. _____ |
| 3. ----- | 7. _____ |
| 4. ----- | 8. _____ |

Present nondrug management (physiotherapy, music therapy, massage etc)

1. -----
2. -----.

## APPENDIX V

### **Karnofsky performance scale:**

**100** Able to carry on normal activity; no special care needed. Normal, no complaints, no evidence of disease.

**90** Able to carry on normal activity, minor signs or symptoms of disease

**80** Normal activity with effort. some signs or symptoms of disease

**70** Cares for self, unable to carry on normal activity or to do active work

**60** Requires occasional assistance from others but able to care for most of his needs

**50** Requires considerable assistance from others and frequent medical care.

**40** Disabled, requires special care and assistance.

**30** Severely disabled, hospitalization indicated, death not imminent

**20** Very sick, hospitalization necessary, active supportive treatment necessary.

**10** Moribound , disease may be rapidly progressing.

**0** Dead.

## APPENDIX VI

Department of Obstetrics and Gynaecology,

Kwara State Specialist Hospital, Sobi, Ilorin.

19<sup>th</sup> October, 2015

The Head of Department,

Department of Surgery,

University of Ilorin Teaching Hospital,

Ilorin.

Dear HOD,

### **LETTER OF PERMISSION**

I am writing to invite patients with breast/gynaecological cancer to participate in my research.

I am studying Palliative Medicine at the University of Cape Town, South Africa.

This research is in partial fulfilment towards the award of Masters Degree in Palliative Medicine.

The study is a descriptive, comparative, cross sectional study exploring the symptom burden and relief of these symptoms among these groups of patients.

I will be using the Memorial Symptom Assessment Scale-Short Form (MSAS-SF) which is a symptom assessment tool, to assess patient symptoms and the degree to which the symptoms cause distress. I will also be using a questionnaire to obtain other information from the patients as well as from the case notes. I will be working with one research assistant.

I will introduce the research study to your staff. The research assistant will be fully trained and knowledgeable regarding the approved protocol. This study will not be beginning until we have full ethical approval.

I am writing to outline some basic study information.

- *Who are we recruiting?*

We are recruiting a total of 100 adult patients with breast or gynaecologic cancer. The patients will be those accessing care at the University of Ilorin Teaching Hospital.

- *How will patients be approached to ask them if they want to take part?*

We ask that your staff identify patients who meet the criteria, and then explain that we are recruiting to a study using questionnaires that ask about their health that would last about 15-20 minutes. If patients are interested in taking part a researcher will speak to them and give further information. If they agree to take part, the researcher will ask for informed consent. The study is entitled ‘an exploration of symptom burden in breast and gynaecological cancer patients accessing care at University of Ilorin Teaching Hospital’. The questionnaire is a composite one with 4 parts: A validated tool called Memorial Symptom Assessment Scale, a table to document symptoms relieved/not relieved and the degree of relief, the third part that would document information extracted from the case notes and the fourth part that involves repeat of the Memorial Symptom Assessment Scale after a week’s interval.



- *How will data collection happen?*

The researcher will then conduct the interview if the patient has given consent. The researcher will hold and store the data in a locked store and will keep the personal information (e.g. name) separate from the questionnaire data. The patient's name will not appear on the questionnaire which will only have a study number as an identifier.

- *What if a patient becomes distressed?*

All respondents will have the opportunity to halt the interview at any time, and will have debriefing (i.e. time to talk without data being collected) at the end of the interview. If the researcher is concerned about respondent distress, they will inform one of the clinical team and will let the patient know that they are doing so.

- *What are the responsibilities of the study site?*

We are asking you to assist in identifying patients who meet the study criteria and to introduce them to the researcher who will discuss the research with them and ask for their informed consent.

We are also asking that should a patient become distressed during the interview that your counselling staff would be prepared to provide the necessary support for the participant. We have found in previous studies that participants welcome the opportunity to respond to questions asked in the Patient Outcome Score and that distress is infrequent. Please would you note your agreement to provide this support when you respond to our request to conduct research within your facility. If you do not have the resources to provide counselling support, we will identify a counsellor who can be on call if required, should a participant express distress or should the researcher identify possible distress.

- *What about study feedback?*

We will liaise closely with you to let you know the number of interviews complete and the remaining interviews needed. We will also produce a dissemination brief on the findings for display within your service, and this will be written in lay language.

We look forward to working with you and fixing the date for launch once we have full ethical approval and translated materials.

Please don't hesitate to contact me should you require further information in the meantime. I will remain the Principal Investigator throughout the study, and encourage you to raise any thoughts with my research assistant or with me. You may raise any ethical concerns with the UITH ERC.

Yours sincerely,

Dr Isiaka-Lawal Salamat.

[Salamat.lawal@gmail.com](mailto:Salamat.lawal@gmail.com)

08039124662

Department of Obstetrics and Gynaecology,  
Kwara State Specialist Hospital, Sobi, Ilorin.  
19<sup>th</sup> October, 2015

The Head of Department,  
Department of Obstetrics & Gynaecology,  
University of Ilorin Teaching Hospital,  
Ilorin.

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- *What are the responsibilities of the study site?*

We are asking you to assist in identifying patients who meet the study criteria and to introduce them to the researcher who will discuss the research with them and ask for their informed consent.

We are also asking that should a patient become distressed during the interview that your counselling staff would be prepared to provide the necessary support for the participant. We have found in previous studies that participants welcome the opportunity to respond to questions asked in the Patient Outcome Score and that distress is infrequent. Please would you note your agreement to provide this support when you respond to our request to conduct research within your facility. If you do not have the resources to provide counselling support, we will identify a counsellor who can be on call if required, should a participant express distress or should the researcher identify possible distress.

- *What about study feedback?*

We will liaise closely with you to let you know the number of interviews complete and the remaining interviews needed. We will also produce a dissemination brief on the findings for display within your service, and this will be written in lay language.

We look forward to working with you and fixing the date for launch once we have full ethical approval and translated materials.

Please don't hesitate to contact me should you require further information in the meantime. I will remain the Principal Investigator throughout the study, and encourage you to raise any thoughts with my research assistant or with me. You may raise any ethical concerns with the UITH ERC.

Yours sincerely,

Dr Isiaka-Lawal Salamat.

[Salamat.lawal@gmail.com](mailto:Salamat.lawal@gmail.com)

08039124662

# UNIVERSITY OF ILORIN TEACHING HOSPITAL

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**MRS. OLAJUMOKE ANIFOWOSHE**  
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UITH ERC Protocol Number: ERC PIN/2015/06/0325

UITH ERC Approval Number: ERC PAN/2015/09/1453

Our Ref: UITH/CAT/189/19<sup>A</sup>/288

Date: 03/09/2015

## **A.N EXPLORATION OF SYMPTOM BURDEN AMONG BREAST AND GYNAECOLOGICAL CANCER PATIENTS ACCESSING CARE AT UNIVERSITY OF ILORIN TEACHING HOSPITAL, ILORIN, KWARA STATE, NIGERIA**

UITH Ethical Research Committee (ERC) assigned number: NHREC/02/05/2010

Name of Applicant/Principal Investigator: **DR. ISIAKA-LAWAL SALAMAT AYODELE**

Address of Applicant: Dept. of O&G, Kwara State Specialist Hospital, Sobi.

Date of receipt of application: 30/06/2015

Type of Review: Full Committee Review

Date of full Committee Decision on the Research: 28/07/2015

Date of full Committee Approval: 03/09/2015

### Notice of full Committee Approval

I am pleased to inform you that the research described in the submitted protocol, the consent forms and other participant information materials have been reviewed by the UITH Ethical Review Committee (ERC) and given full Committee approval.

This approval dates from 03/09/2015 to 02/09/2016. You are requested to inform the committee at the commencement of the research to enable it appoint its representative who will ensure compliance with the approved protocol. If there is delay in starting the research, please inform the ERC so that the dates of approval can be adjusted accordingly.

Note that no participant accrual or activity related to this research may be conducted outside these dates.

The UITH ERC requires you to comply with all the institutional guidelines and regulations and ensure that all adverse events are reported promptly to the ERC.

No changes are allowed in the research without prior approval by the ERC. Please note that the ERC reserves the right to conduct monitoring/oversight visit to your research site without prior notification.

Notwithstanding above, we will not be responsible for any misconduct on the part of the researcher in the course of carrying out the research.

Thank you

**Signed**

**PROF. O.T. ADEDOYIN** MBBS (L.) FWACP (Pled.) FRCP (Edin), ASN/ASN Fellow, Cert. EPBM  
Chairman, UITH Ethics Review Committee (ERC)



UNIVERSITY OF CAPE TOWN  
Faculty of Health Sciences  
Human Research Ethics Committee



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11 August 2015

**HREC REF: 570/2015**

**Dr L Gwyther**  
School of Public Health & Family Medicine  
Room 2.26  
Falmouth Building-FHS

Dear Dr Gwyther

**PROJECT TITLE: AN EXPLORATION OF SYMPTOM BURDEN AMONG BREAST AND GYNAECOLOGICAL CANCER PATIENTS ACCESSING CARE AT UNIVERSITY OF ILORIN TEACHING HOSPITAL, ILORIN NIGERIA (Masters-candidate-Dr I Salamat)**

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee (HREC) for review.

It is a pleasure to inform you that the HREC has formally approved the above-mentioned study.

**Approval is granted for one year until the 30th August 2016.**

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.

(Forms can be found on our website: [www.health.uct.ac.za/fhs/research/humanethics/forms](http://www.health.uct.ac.za/fhs/research/humanethics/forms))


**We acknowledge that the following student: Dr Isiaka-lawal Salamat is also involved in this project.**

**Please quote the HREC reference no in all your correspondence.**

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Yours sincerely

**Signed**

 **PROFESSOR M. BLOCKMAN**  
**CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE**  
Federal Wide Assurance Number: FWA00001537.  
Institutional Review Board (IRB) number: IRB00001938



